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I, JONNE YABSLEY, TEAM LEADER EXAMINATION SUPPORT AND SALES hereby certify that annexed is a true copy of the Provisional specification in connection with Application No. 2002952117 for a patent by FUJISAWA PHARMACEUTICAL CO., LTD. as filed on 10 October 2002.

WITNESS my hand this
Twenty-first day of November 2002

J R Yabsley

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Fujisawa Pharmaceutical Co., Ltd.

AUSTRALIA
Patents Act 1990

PROVISIONAL SPECIFICATION
for the invention entitled:

"Cyclic tetrapeptide compound and use thereof"

The invention is described in the following statement:

DESCRIPTION

CYCLIC TETRAPEPTIDE COMPOUND AND USE THEREOF

TECHNICAL FIELD

The present invention relates to a cyclic tetrapeptide compound which is useful as a medicament, to a process for producing the same and to a pharmaceutical composition comprising the same.

BACKGROUND ART

Histone deacetylases are known to play an essential role in the transcriptional machinery for regulating gene expression, and histone deacetylase inhibitors induce histone hyperacetylation and affect the gene expression. Therefore, a histone deacetylase inhibitor is useful as a therapeutic or prophylactic agent for diseases caused by abnormal gene expression, such as inflammatory disorders, diabetes, diabetic complications, homozygous thalassemia, fibrosis, cirrhosis, acute promyelocytic leukaemia (APL), protozoal infection, and the like.

In this connection, a cyclic tetrapeptide compound that can be used as an antitumor agent is disclosed in JP-A-7-196686 but this publication is silent on the action against histone deacetylases and the effect against the above-mentioned various diseases.

DISCLOSURE OF THE INVENTION

The present invention relates to a novel cyclic tetrapeptide compound which is useful as a medicament, to a process for producing the same and to a pharmaceutical composition comprising the same.

More particularly, it relates to a cyclic tetrapeptide compound which has a potent inhibitory effect on the activity of histone deacetylase.

The inventors of the present invention also found that a histone deacetylase inhibitor, such as cyclic tetrapeptide compound of formula (I) (hereinafter cyclic tetrapeptide compound [I] or compound [I]), has a potent immunosuppressive effect and potent antitumor effect. Therefore, a histone deacetylase inhibitor, such as cyclic tetrapeptide compound [I], is useful as an active ingredient of an immunosuppressant and an antitumor

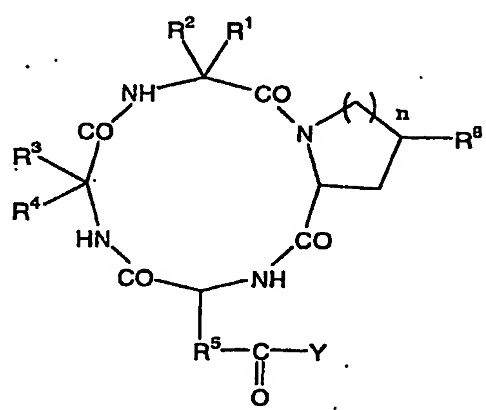
agent and useful as a therapeutic or prophylactic agent for an organ transplant rejection, autoimmune diseases, tumor, and the like.

Accordingly, one object of the present invention is to provide a compound which has biological activities as stated above.

A further object of the present invention is to provide a pharmaceutical composition containing, as an active ingredient, the cyclic tetrapeptide compound [I].

A yet further object of the present invention is to provide a use of the histone deacetylase inhibitors, such as cyclic tetrapeptide compound [I], for treating and preventing diseases stated above.

Thus, the present invention provides a cyclic tetrapeptide compound of the formula (I):



(I)

wherein

R^1 is hydrogen,

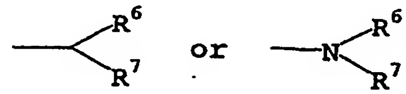
R^2 is lower alkyl, aryl, ar(lower)alkyl optionally substituted with one or more suitable substituent(s), heterocyclic(lower)alkyl or cyclo(lower)alkyl(lower)alkyl,

R^3 and R^4 are each independently hydrogen, lower alkyl, ar(lower)alkyl optionally substituted with one or more suitable substituent(s), heterocyclic(lower)alkyl optionally substituted with one or more suitable substituent(s) or cyclo(lower)alkyl(lower)alkyl, or

R^3 and R^4 are linked together to form lower alkylene or condensed ring,

R^5 is lower alkylene wherein at least one methylene of which is

optionally replaced by oxygen atom(s), or lower alkenylene, Y is hydroxy, aryl,



[wherein R^6 is hydrogen, halogen, hydroxy or protected hydroxy, and R^7 is hydrogen, halogen or lower alkyl], R^8 is hydrogen or lower alkyl, and n is an integer of 1 or 2, providing that, when R^3 is methyl, R^4 is methyl or ethyl, R^5 is pentylene and Y is 1-hydroxyethyl, then R^2 is phenyl(lower)alkyl substituted with one or more suitable substituent(s), or a salt thereof.

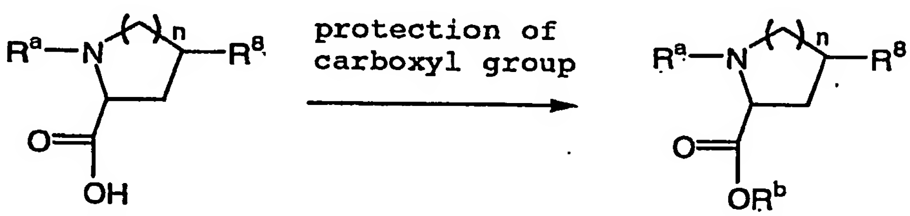
The compound [I] and a salt thereof can be prepared by the process as illustrated in the following reaction schemes.

The compound [I] of the present invention may be prepared by a liquid phase method (i.e. Preparation A → Preparation C → Examples) or a solid phase-liquid phase relay method (i.e. Preparation B → Preparation C → Examples).

Hereinafter, the processes for preparing the compound [I] of the present invention are explained in detail.

Preparation A

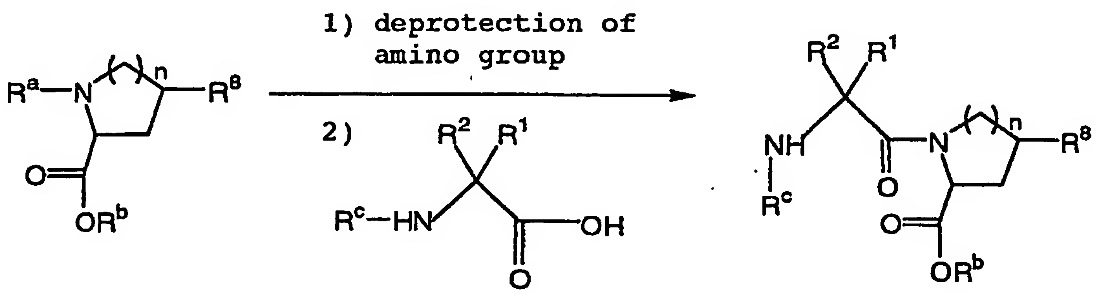
Preparation A-1



(a-1) or a salt thereof

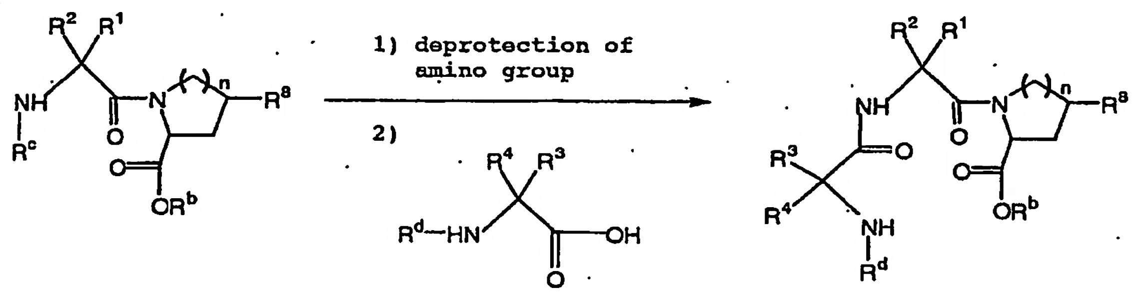
(a-2) or a salt thereof

Preparation A-2



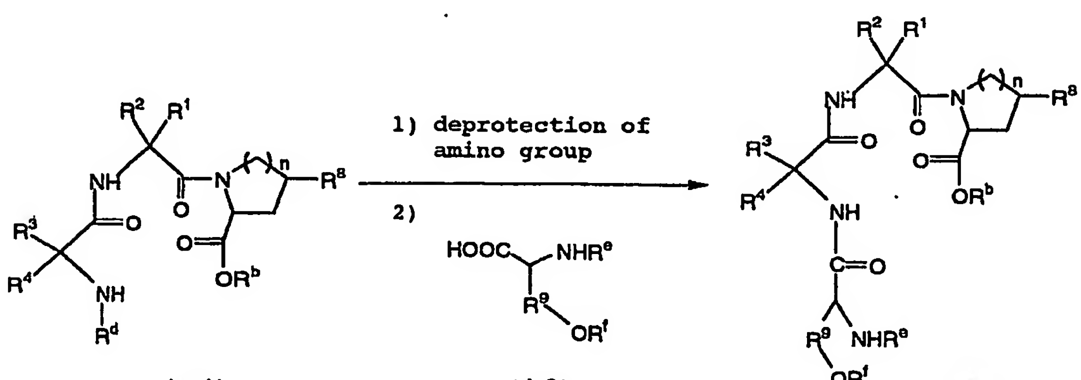
(a-2) or a salt thereof | (d-1) or a salt thereof | (a-3) or a salt thereof

Preparation A-3



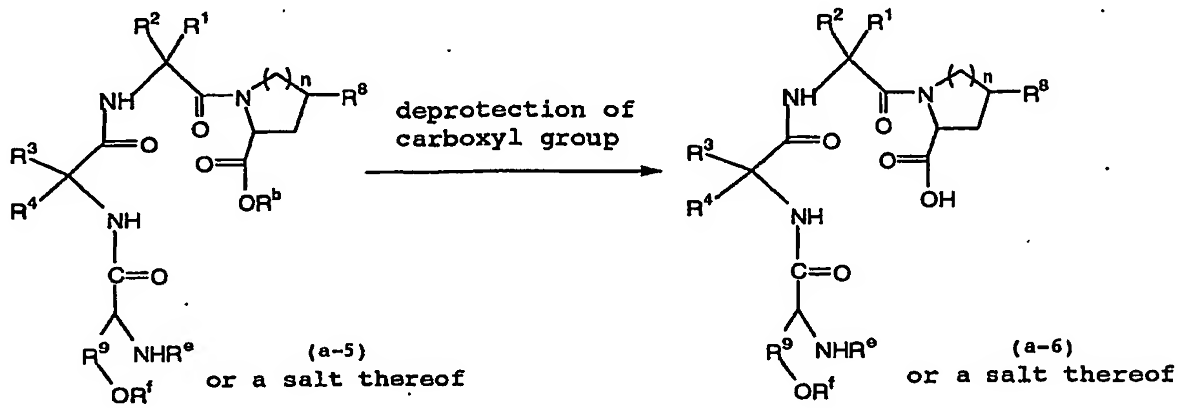
(a-3) or a salt thereof | (d-2) or a salt thereof | (a-4) or a salt thereof

Preparation A-4



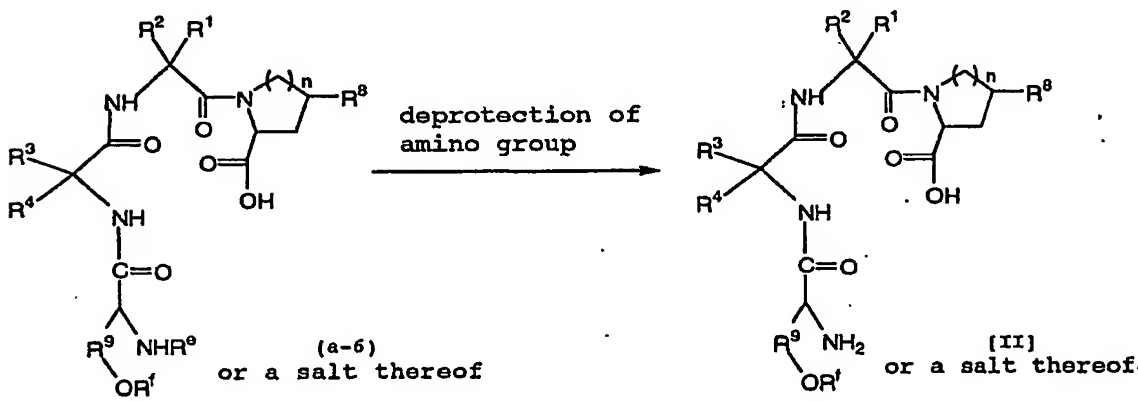
(a-4) or a salt thereof | (d-3) or a salt thereof | (a-5) or a salt thereof

Preparation A-5



(a-5) or a salt thereof → (a-6) or a salt thereof

Preparation A-6



(a-6) or a salt thereof → [II] or a salt thereof.

wherein
R^1, R^2, R^3, R^4, R^8 and n are as defined above,
R^9 is lower alkylene,
R^a is hydrogen or amino protective group,
R^b is carboxy protective group,
R^c, R^d and R^e are each independently amino protective group, and
R^f is hydroxy protective group.

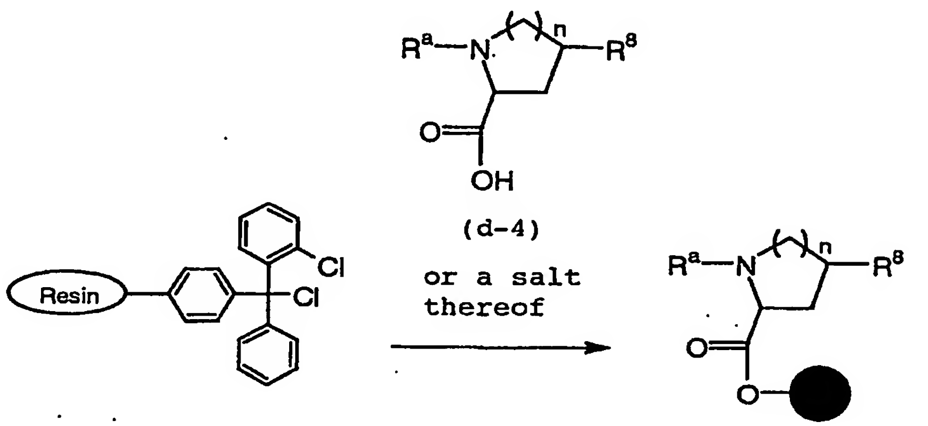
In the above Preparation A, the deprotection of carboxyl group is exemplified by Preparation 17 and the like, and the deprotection of amino group is exemplified by Preparation 18 and the like.

Alternatively, the deprotection of carboxyl and amino groups may be conducted simultaneously (e.g. Preparation 53,

Preparation 57 and the like).

Preparation B

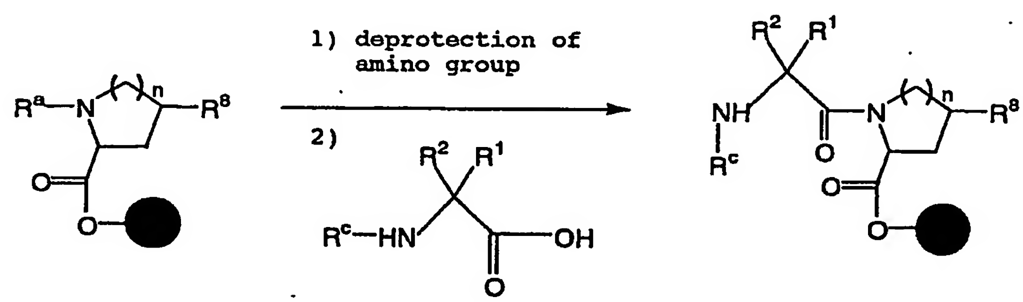
Preparation B-1



(b-1) or a salt thereof

(b-2) or a salt thereof.

Preparation B-2

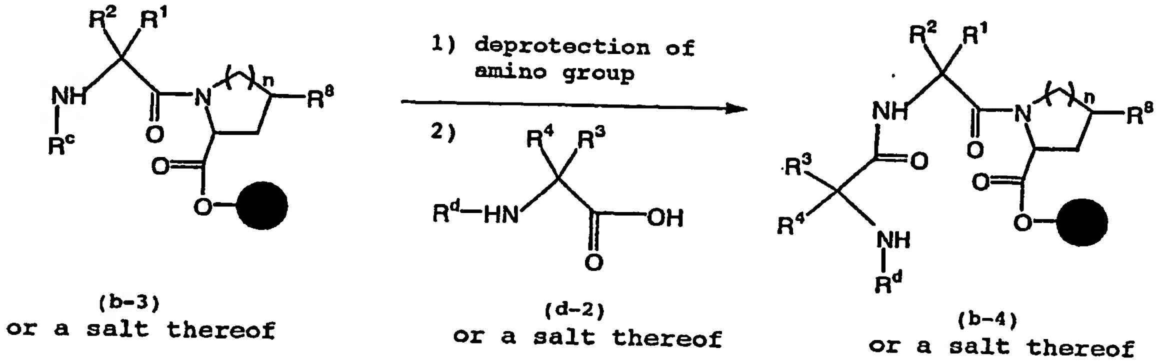


(b-2) or a salt thereof

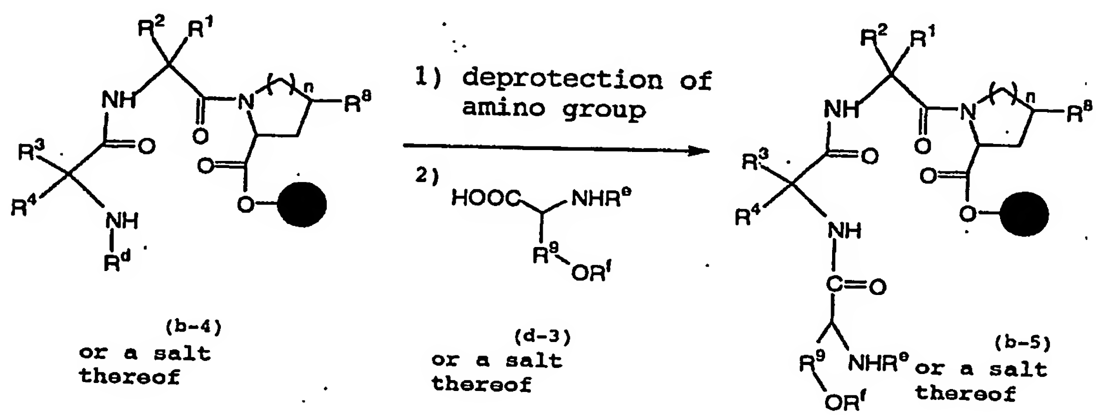
(d-1) or a salt thereof

(b-3) or a salt thereof

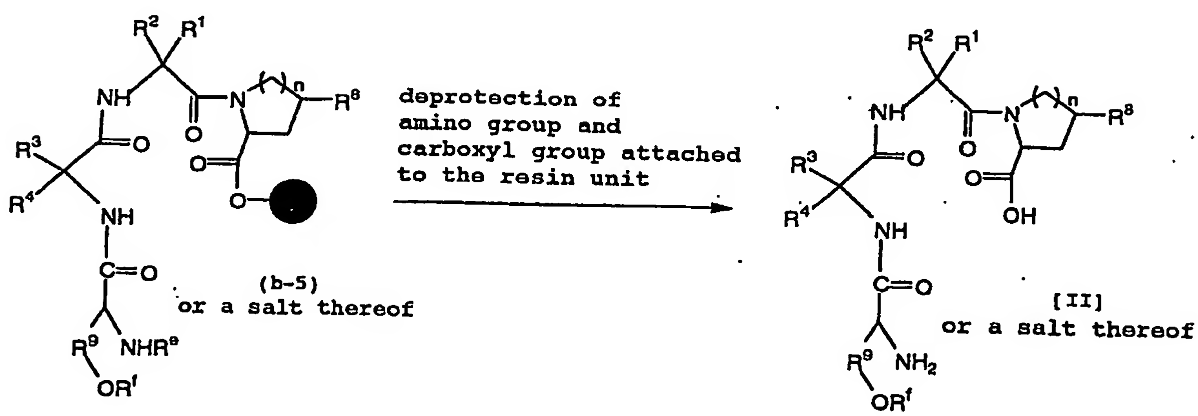
Preparation B-3



Preparation B-4

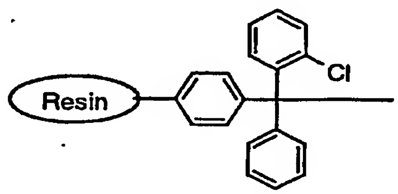


Preparation B-5



wherein
R^1, R^2, R^3, R^4, R^8 and n are as defined above,
R^9 is lower alkylene,
R^a is hydrogen or amino protective group,
R^c, R^d and R^e are each independently amino protective group,
R^f is hydroxy protective group, and

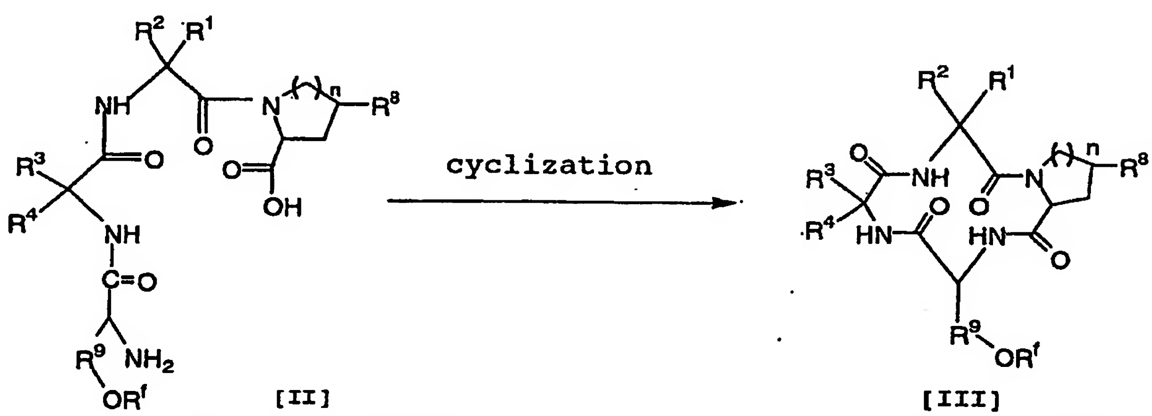
 is the following resin unit:



wherein  is a resin,

Preparation C

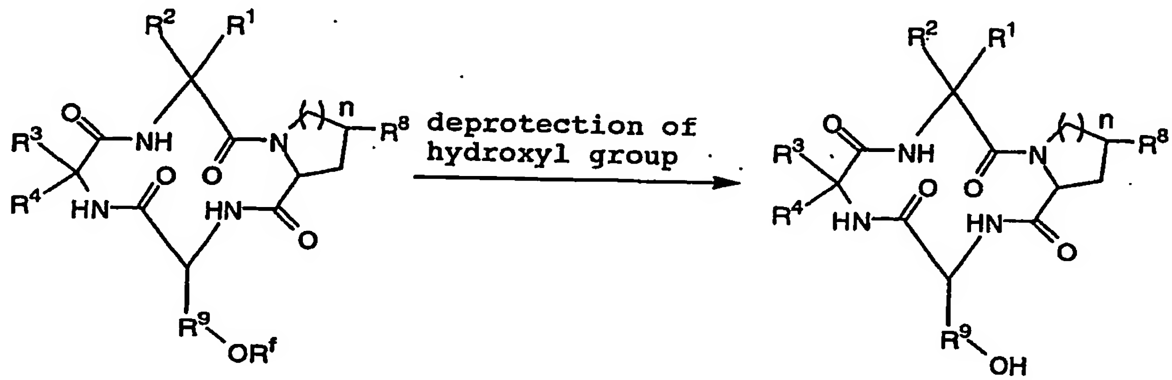
Preparation C-1



[II] or a salt thereof

[III] or a salt thereof

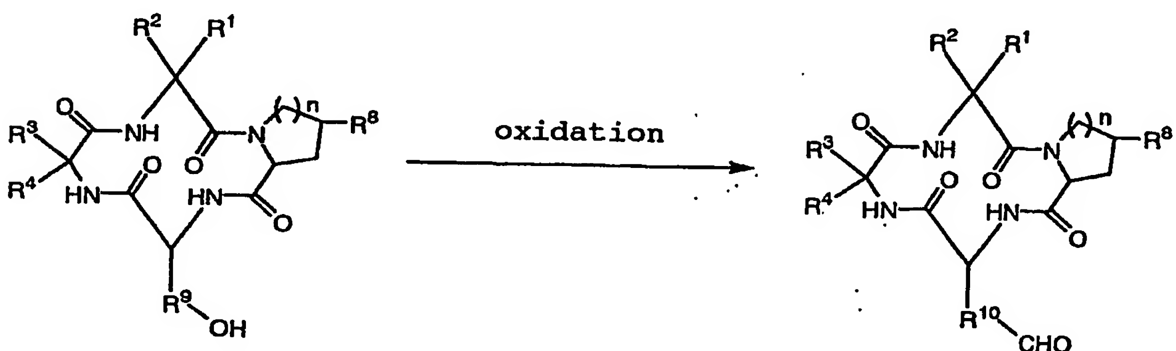
Preparation C-2



[III]
or a salt thereof

[IV]
or a salt thereof

Preparation C-3



[IV]
or a salt thereof

[V]
or a salt thereof

wherein

R^1, R^2, R^3, R^4, R^8 and n are as defined above,

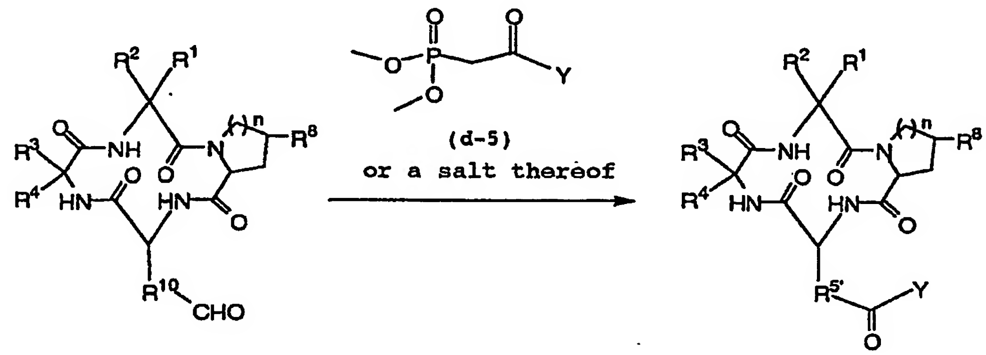
R^9 and R^{10} are each independently lower alkylene, and

R^f is a hydroxy protective group.

The compound [V] obtained from the Preparation C is used in the preparation of the compound [I] of the present invention.

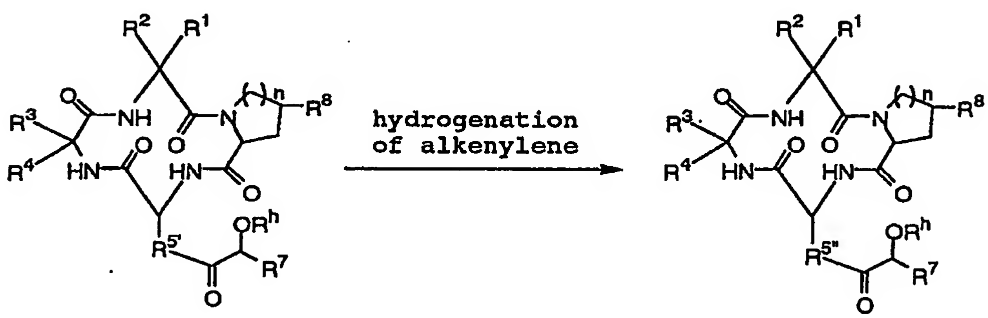
Preparation of the compound [I] of the present invention

Preparation of the compound [I-1]



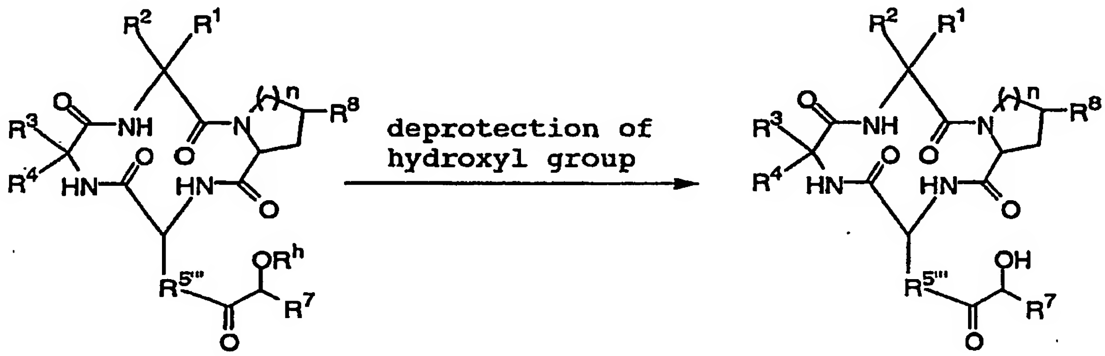
[V] or a salt thereof → [I-1] or a salt thereof

Preparation of the compound [I-2]



[I-1'] or a salt thereof → [I-2] or a salt thereof

Preparation of the compound [I-3]



[I-1] or [I-2]
or a salt thereof

[I-3]
or a salt thereof

wherein

R^1, R^2, R^3, R^4, R^7, R^8, R^9 and n are as defined above,

$R^{5'}$ is lower alkenylene,

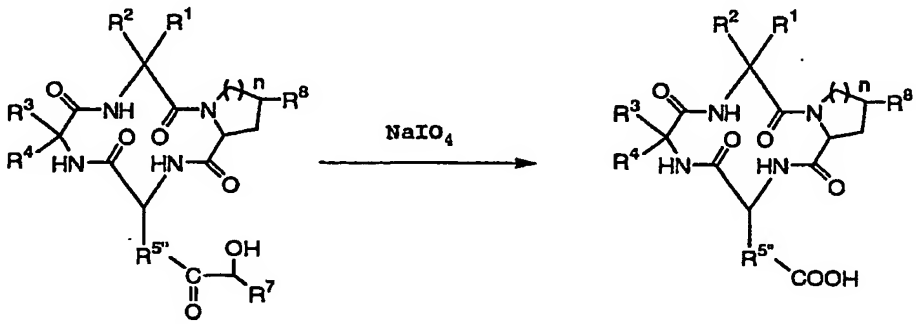
$R^{5''}$ is lower alkylene,

$R^{5'''}$ is lower alkylene or lower alkenylene, and

R^h is hydroxy protective group.

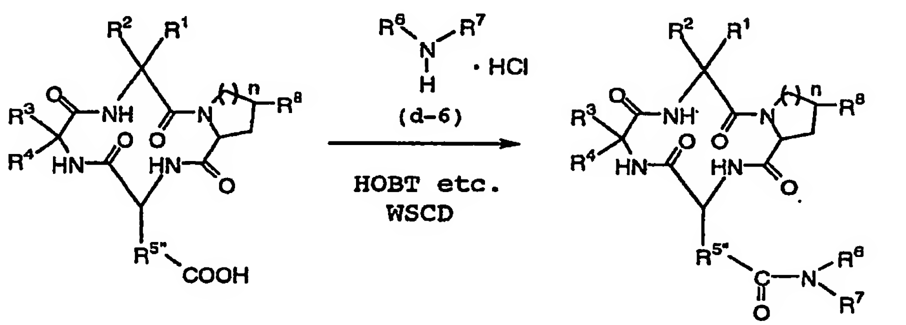
To determine absolute configuration of the hydroxyl group of the compound [I-3] and to estimate optical purity of the isomer of the compound [I-3], the compound [I-3] is reacted with a reagent such as (R or S)-(+ or −)-α-methoxy-α-trifluoromethyl-α-phenylacetyl chloride, 1-naphthylmethoxyacetic acid, 2-naphthylmethoxyacetic acid, 9-anthrylmethoxyacetic acid, 2-anthrylmethoxyacetic acid, and the like. This reaction is exemplified by Example 53.

Preparation of the compound [I-4]



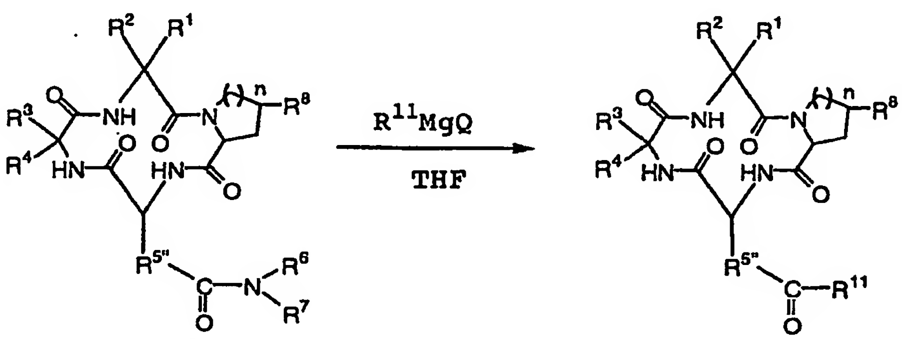
[I-3'] or a salt thereof — [I-4] or a salt thereof

Preparation of the compound [I-5]



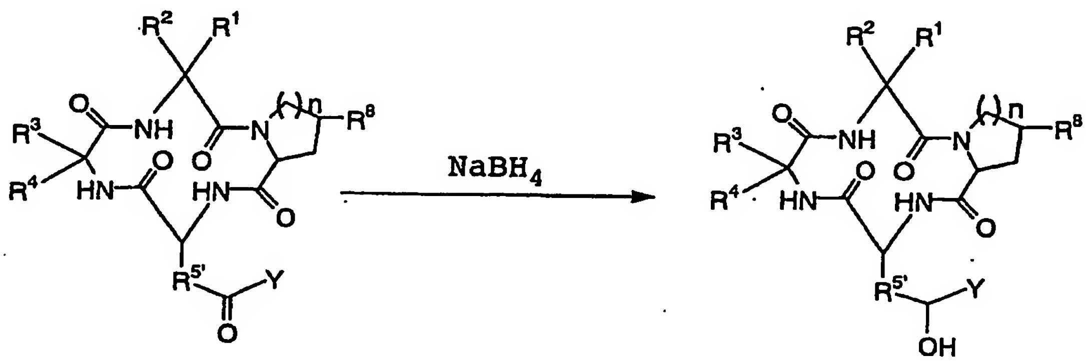
[I-4] or a salt thereof — [I-5] or a salt thereof

Preparation of the compound [I-6]



[I-5] or a salt thereof — [I-6] or a salt thereof

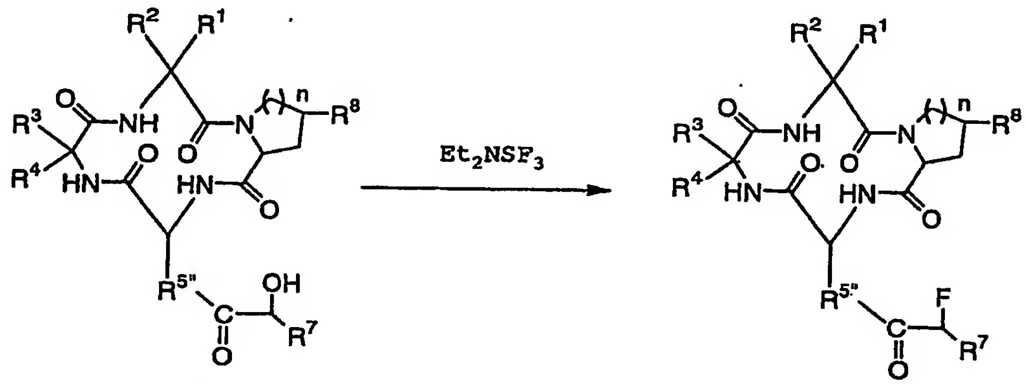
Preparation of the compound [I-7]



[I-1] or a salt thereof

[I-7] or a salt thereof

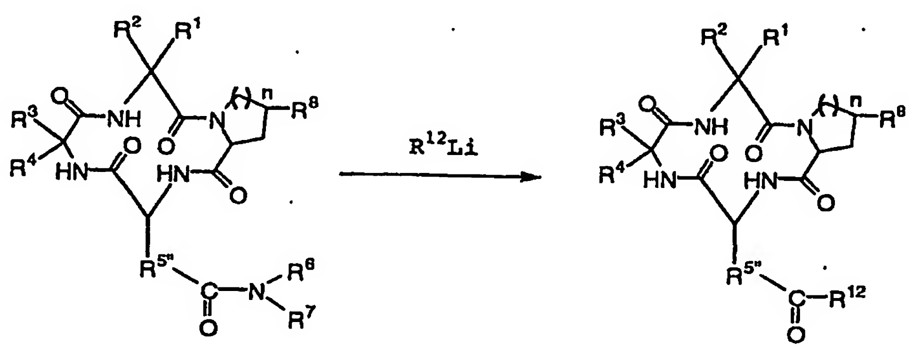
Preparation of the compound [I-8]



[I-3'] or a salt thereof

[I-8] or a salt thereof

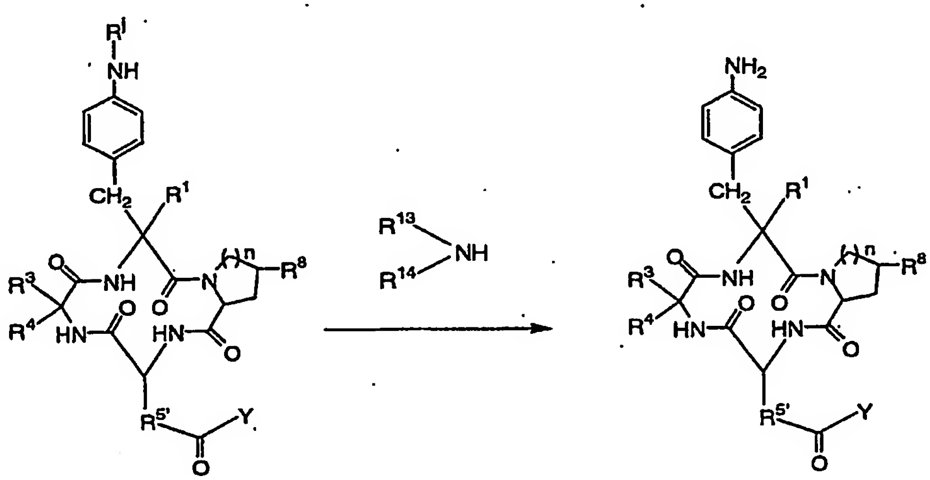
Preparation of the compound [I-9]



[I-5] or a salt thereof

[I-9] or a salt thereof

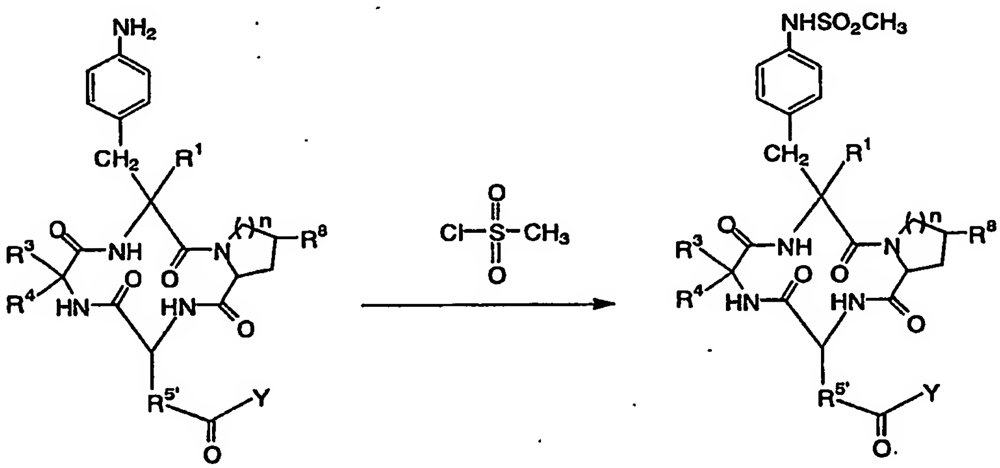
Preparation of the compound [I-10]



[I-1''] or a salt thereof

[I-10] or a salt thereof

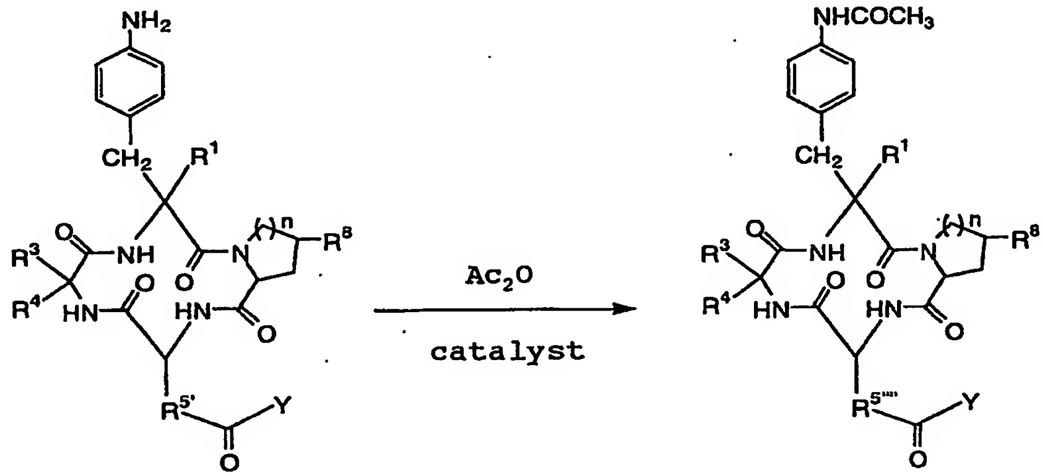
Preparation of the compound [I-11]



[I-10] or a salt thereof

[I-11] or a salt thereof

Preparation of the Compound [I-12]



[I-10]
or a salt thereof

[I-12]
or a salt thereof

wherein

R^1, R^2, R^3, R^4, $R^{5'}$, $R^{5''}$, $R^{5'''}$, R^6, R^7, R^8, R^9, R^{10}, Y and n are as defined above,

$R^{5''''}$ is lower alkylene wherein at least one methylene of which is replaced by oxygen atom(s),

R^{11} is lower alkyl, aryl or ar(lower)alkyl,

R^{12} is lower alkyl, lower alkenyl or aryl and the like,

R^{13} and R^{14} are each independently lower alkyl or lower cycloalkyl, or

R^{13} and R^{14} are linked together with the adjacent nitrogen atom to form a ring wherein one or more methylene(s) of the ring is(are) optionally replaced by heteroatom(s) selected from an oxygen atom, a nitrogen atom and a sulfur atom,

Q is halogen, and

R^j is amino protective group.

Suitable "salt" is a pharmaceutically acceptable and conventional non-toxic salt, and may include a salt with a base or an acid addition salt such as a salt with an inorganic base, for example, an alkaline metal salt (e.g., sodium salt, potassium salt, and the like), an alkaline earth metal salt (e.g., calcium salt, magnesium salt, and the like), an ammonium salt; a salt with an organic base, for example, an organic amine salt

(e.g., triethylamine salt, diisopropylethylamine salt, pyridine salt, picoline salt, ethanolamine salt, triethanolamine salt, dicyclohexylamine salt, N,N'-dibenzylethylenediamine salt, and the like);

an inorganic acid addition salt (e.g., hydrochloride, hydrobromide, sulfate, phosphate, and the like);

an organic carboxylic sulfonic acid addition salt (e.g., formate, acetate, trifluoroacetate, maleate, tartrate, fumarate, methanesulfonate, benzenesulfonate, toluenesulfonate, and the like); and

a salt with a basic or acidic amino acid (e.g., arginine, aspartic acid, glutamic acid, and the like).

Suitable examples and illustration of the various definitions in the above and subsequent descriptions, which the present invention intends to be included within the scope thereof, are explained in detail as follows:

The term "halogen" means fluorine, chlorine, bromine, and iodine.

The term "lower" used in the description is intended to mean 1 to 6 carbon atoms, unless otherwise indicated.

Suitable example of "one or more" may be the number of 1 to 6, preferably 1 to 3.

Suitable example of "lower alkyl" may include straight or branched one having 1 to 6 carbon atom(s), such as methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, tert-butyl, pentyl, tert-pentyl, neopentyl, hexyl, isohexyl and the like. The preferred lower alkyl for R^2 may be 2-methyl-1-propyl, the preferred lower alkyl for R^3 and R^4 may be methyl, ethyl and isopropyl, the preferred lower alkyl for R^7 may be methyl and ethyl, and the preferred lower alkyl for R^8 may be methyl.

Suitable example of "lower alkylene" may include straight or branched one having 1 to 6 carbon atom(s), such as methylene, ethylene, trimethylene, propylene, tetramethylene, pentamethylene, hexamethylene and the like. The preferred lower alkylene for R^3 and R^4 may be tetramethylene.

Suitable example of "lower alkylene wherein at least one methylene of which is optionally replaced by oxygen atom(s)" may be pentamethylene, tetramethyleneoxy and the like, in which the preferred one for R^5 may be pentamethylene.

Suitable example of "lower alkenylene" may include straight or branched one having 1 to 6 carbon atom(s), such as ethenylene, 1-propenylene, 2-propenylene, 2-methyl-1-propenylene, 2-methyl-2-propenylene, 1-butenylene, 2-butenylene, 3-butenylene, 1-pentenylene, 2-pentenylene, 3-pentenylene, 4-pentenylene, 1-hexenylene, 2-hexenylene, 3-hexenylene, 4-hexenylene, 5-hexenylene and the like, in which the preferred one for R^5 may be 1-pentenylene.

Suitable example of "aryl" may include C_6-C_{16} aryl such as phenyl, naphthyl, anthryl, pyrenyl, phenanthryl, azulenyl and the like, preferably phenyl, naphthyl. The preferred one for R^2 may be phenyl, and the preferred one for Y may be phenyl.

Suitable example of ar(lower)alkyl for R^2 may include phenyl(C_1-C_6)alkyl such as benzyl, phenethyl, phenylpropyl, phenylbutyl, phenylhexyl and the like, naphthyl(C_1-C_6)alkyl such as naphthylmethyl, naphthylethyl, naphthylpropyl, naphthylbutyl, naphthylpentyl, naphtylhexyl and the like. The preferred one for R^2 may be phenyl(C_1-C_6)alkyl, more preferably benzyl.

Suitable example of "suitable substituent(s)" of "ar(lower)alkyl optionally substituted with one or more suitable substituent(s)" for R^2 may include lower alkyl, lower alkoxy, ar(lower)alkyloxy, cyano, hydroxy, halogen, amino, lower alkanoylamino, methanesulfonylamino, phenyl, and the like.

Suitable "heterocyclic" in the terms of "heterocyclic(lower)alkyl" for R^2 may include 5- or 6-membered heteromonocyclic group or condensed heterocyclic group, each of which contains at least one heteroatom(s) selected from a sulfur atom, an oxygen atom and a nitrogen atom.

Suitable 5- or 6-membered heteromonocyclic group containing at least one heteroatom(s) selected from a sulfur atom, an oxygen atom and a nitrogen atom include, for example, pyridyl, dihydropyridyl, azepinyl (e.g., 1H-azepinyl and the like), pyrrolyl, pyrrolinyl, imidazolyl, pyrazolyl, pyrimidinyl, pyrazinyl, pyridazinyl, triazolyl (e.g., 4H-1,2,4-triazolyl, 1H-1,2,3-triazolyl, 2H-1,2,3-triazolyl and the like), tetrazolyl (e.g., 1H-tetrazolyl, 2H-tetrazolyl and the like), perhydroazepinyl (e.g., perhydro-1H-azepinyl and the like), pyrrolidinyl, imidazolidinyl, piperidyl, piperadinyl, oxazolyl,

isoxazolyl, oxadiazolyl (e.g., 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl, 1,2,5-oxadiazolyl and the like), morpholinyl, sydnonyl, thiazolyl, isothiazolyl, thiadiazolyl (e.g., 1,2,3-thiazidiazolyl, 1,2,4-thiadiazolyl, 1,3,4-thiadiazolyl, 1,2,5-thiadiazolyl and the like), dihydrothiazinyl, thiazolidinyl, furyl, dihydrooxatiinyl and the like.

Suitable condensed heterocyclic group containing at least one heteroatom(s) selected from a sulfur atom, an oxygen atom and a nitrogen atom include, for example, indolyl, isoindolyl, indolidinyl, benzimidazolyl, quinolyl, isoquinolyl, indazolyl, benzotriazolyl, quinoxalinyl, imidazopyridyl (e.g., imidazo[4,5-c]pyridyl and the like), tetrahydroimidazopyridyl (e.g., 4,5,6,7-tetrahydro[4,5-c]pyridyl and the like), 7-azabicyclo[2.2.1]heptyl, 3-azabicyclo[3.2.2]nonanyl, benzoxazolyl, benzoxadiazolyl, benzothiazolyl, benzothiadiazolyl, benzothienyl, benzodithiinyl, benzoxathiinyl and the like.

Among these, the preferable "heterocyclic" in the terms of "heterocyclic(lower)alkyl" for R^2 include, for example, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, thienyl, furyl, quinolyl, imidazolyl, indolyl and the like. The preferred "heterocyclic(lower)alkyl" for R^2 may be 2-pyridylmethyl, 4-pyridylmethyl, 3-indolylmethyl and the like.

Suitable "cyclo(lower)alkyl" moiety in the terms of "cyclo(lower)alkyl(lower)alkyl" for R^2 may be cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and the like. The preferred "cyclo(lower)alkyl(lower)alkyl" for R^2 may be cyclopropylmethyl, cyclobutylmethyl, cyclopentylmethyl, cyclohexylmethyl, cyclopropylethyl, cyclobutylethyl, cyclopentylethyl, cyclohexylethyl and the like.

Suitable "ar(lower)alkyl" for R^3 and R^4 may include phenyl(lower)alkyl [e.g. phenyl(C_1-C_6)alkyl such as benzyl, phenethyl, phenylpropyl, phenylbutyl, phenylhexyl and the like], naphthyl(lower)alkyl [e.g. naphthyl(C_1-C_6)alkyl such as naphthylmethyl, naphthylethyl, naphthylpropyl, naphthylbutyl, naphthylhexyl and the like], and the like. The preferred one for R^2 may be phenyl(C_1-C_6)alkyl, more preferably benzyl.

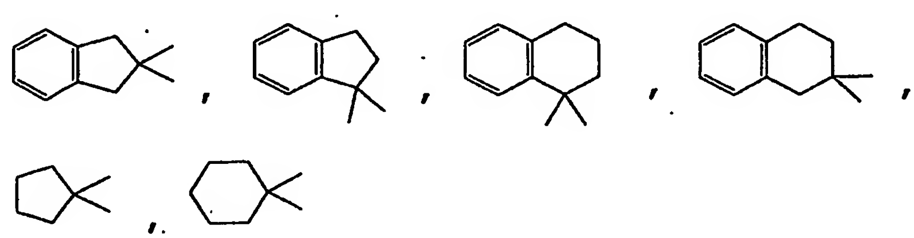
Suitable example of "suitable substituent(s)" of

"ar(lower)alkyl optionally substituted with one or more suitable substituent(s)" for R^3 and R^4 may include lower alkoxy, lower alkyl, cyano, halogen, amino, nitro, carboxy and the like. The preferred "ar(lower)alkyl optionally substituted with one or more suitable substituent(s)" for R^3 and R^4 may include (4-methoxyphenyl)methyl, (4-ethoxyphenyl)methyl and the like. Suitable "heterocyclic(lower)alkyl" for R^3 and R^4 may include, for example, indenylmethyl, pyridylmethyl, thienylmethyl, furylmethyl, imidazolylmethyl and the like.

Suitable example of "suitable substituent(s)" of "heterocyclic(lower)alkyl optionally substituted with one or more suitable substituent(s)" for R^3 and R^4 may be methyl, ethyl, alkoxy, cyano, halogen and the like, and the preferred "heterocyclic(lower)alkyl optionally substituted with one or more suitable substituent(s)" for R^3 and R^4 may include N-methyl-2-indenylmethyl and the like.

Suitable example of "cyclo(lower)alkyl(lower)alkyl" for R^3 and R^4 may be cyclohexylmethyl, cyclopentylmethyl and the like.

Suitable example of "condensed ring" for R^3 and R^4 may be, for example,



and the like.

Suitable "lower alkyl" for R^{11} may be methyl, ethyl and the like, suitable "aryl" for R^{11} may be C_6-C_{12} aryl such as phenyl and the like, and suitable "ar(lower)alkyl" for R^{11} may be $(C_6$-$C_{12})$aryl$(C_1$-$C_6)$alkyl such as benzyl and the like.

Suitable "lower alkyl" for R^{12} may be methyl, ethyl, propyl (e.g., isopropyl and the like), butyl (e.g., isobutyl, t-butyl and the like), hexyl (e.g., n-hexyl) and the like, suitable "lower alkenyl" for R^{12} may be vinyl and the like, and suitable "aryl" for R^{12} may be C_6-C_{12} aryl such as phenyl and the like.

Suitable "lower alkyl" for R^{13} and R^{14} may be lower alkyl

(e.g., methyl, ethyl and the like) and suitable "lower cycloalkyl" for R^{13} and R^{14} may be cyclohexyl and the like.

Suitable "ring" of the "ring wherein one or more methylene(s) of the ring is(are) optionally replaced by heteroatom(s) selected from an oxygen atom, a nitrogen atom and a sulfur atom" for R^{13} and R^{14} may be piperidino, morpholino and the like.

Suitable carboxy protective group may include:
lower alkyl (e.g. methyl, ethyl, propyl, isopropyl, butyl, isobutyl, t-butyl, pentyl, hexyl and the like), preferably methyl, ethyl and t-butyl;
mono(or di or tri)halo(lower)alkyl (e.g. 2-iodoethyl, 2,2,2-trichloroethyl and the like), preferably 2,2,2-trichloroethyl;
lower alkanoyloxy(lower)alkyl (e.g. acetoxymethyl, propionyloxymethyl, butyryloxymethyl, valeryloxymethyl, pivaloyloxymethyl, hexanoyloxymethyl, 1(or 2)-acetoxyethyl, 1(or 2 or 3)-acetoxypropyl, 1(or 2 or 3 or 4)-acetoxybutyl, 1(or 2)-propionyloxyethyl, 1(or 2 or 3)-propionyloxypropyl, 1(or 2)-butyryloxyethyl, 1(or 2)-isobutyryloxyethyl, 1(or 2)-pivaloyloxyethyl, 1(or 2)-hexanoyloxyethyl, isobutyryloxymethyl, 2-ethylbutyryloxymethyl, 3,3-dimethylbutyryloxymethyl, 1(or 2)-pentanoyloxyethyl, and the like);
lower alkanesulfonyl(lower)alkyl (e.g. 2-mesylethyl and the like);
lower alkoxycarbonyloxy(lower)alkyl (e.g. methoxycarbonyloxymethyl, ethoxycarbonyloxymethyl, 2-methoxycarbonyloxyethyl, 1-ethoxycarbonyloxyethyl, 1-isopropoxycarbonyloxyethyl, and the like);
[5-(lower)alkyl-2-oxo-1,3-dioxol-4-yl](lower)alkyl (e.g. (5-methyl-2-oxo-1,3-dioxol-4-yl)methyl, (5-ethyl-2-oxo-1,3-dioxol-4-yl)methyl, (5-propyl-2-oxo-1,3-dioxol-4-yl)methyl, and the like);
aryl optionally substituted with one or more suitable substituent(s) (e.g. phenyl, o(or m or p)-chlorophenyl, tolyl, o(or m or p)-t-butylphenyl, xylyl, mesityl, cumenyl, and the like);
ar(lower)alkyl in which the aryl portion is optionally substituted with one or more suitable substituent(s) (e.g. benzyl, p-methoxybenzyl, o(or p)-nitrobenzyl, phenethyl, trityl, benzhydryl, bis(methoxyphenyl)methyl, m,p-dimethoxybenzyl, 4-

hydroxy-3,5-di-t-butylbenzyl, and the like), preferably benzyl, p-methoxybenzyl and o(or p)-nitrobenzyl;
arylcarbonyl(lower)alkyl in which the aryl portion is optionally substituted with one or more suitable substituent(s) (e.g. phenacyl and the like);
cyclo(lower)alkyl (e.g. cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and the like);
lower alkenyl (e.g. vinyl, allyl, and the like), preferably allyl;
lower alkynyl (e.g. ethynyl, propynyl, and the like);
trisubstituted silyl such as tri(lower)alkylsilyl (e.g. trimethylsilyl, triethylsilyl, tributylsilyl, tert-butyldimethylsilyl, tri-tert-butylsilyl, and the like), lower alkyldiarylsilyl (e.g. methyldiphenylsilyl, ethyldiphenylsilyl, propyldiphenylsilyl, tert-butyldiphenylsilyl, and the like), and the like, preferably trimethylsilyl, triethylsilyl, tert-butyldimethylsilyl and tert-butyldiphenylsilyl;
tri(lower)alkylsilyl(lower)alkyl (e.g. 2-(trimethylsilyl)ethyl and the like);
1-(lower)alkyl-2,6,7-trioxabicyclo[2.2.2]oct-4-yl (e.g. 1-methyl-2,6,7-trioxabicyclo[2.2.2]oct-4-yl, 1-ethyl-2,6,7-trioxabicyclo[2.2.2]oct-4-yl, and the like); and the like.

Suitable hydroxy protective group may include:
lower alkyl such as methyl, ethyl, propyl, isopropyl, butyl, isobutyl, t-butyl, pentyl, hexyl, and the like, preferably methyl;
lower alkoxy(lower)alkyl (e.g. methoxymethyl and the like);
lower alkoxy(lower)alkoxy(lower)alkyl (e.g. 2-methoxyethoxymethyl and the like);
ar(lower)alkyl in which the aryl portion is optionally substituted with one or more suitable substituent(s) (e.g. benzyl, p-methoxybenzyl, m,p-dimethoxybenzyl, and the like), preferably benzyl;
ar(lower)alkoxy(lower)alkyl in which the aryl portion is optionally substituted with one or more suitable substituent(s) (e.g. benzyloxymethyl, p-methoxybenzyloxymethyl, and the like);
(lower)alkylthio(lower)alkyl (e.g. methylthiomethyl, ethylthiomethyl, propylthiomethyl, isopropylthiomethyl, butylthiomethyl, isobutylthiomethyl, hexylthiomethyl, and the

like), and the like, preferably methylthiomethyl;
trisubstituted silyl such as tri(lower)alkylsilyl (e.g. trimethylsilyl, triethylsilyl, tributylsilyl, tert-butyldimethylsilyl, tri-tert-butylsilyl, and the like), lower alkyldiarylsilyl (e.g. methyldiphenylsilyl, ethyldiphenylsilyl, propyldiphenylsilyl, tert-butyldiphenylsilyl, and the like), and the like, preferably tert-butyldimethylsilyl and tert-butyldiphenylsilyl;
acyl as described below [e.g. aliphatic acyl such as lower alkanoyl (e.g. acetyl, propanoyl, pivaloyl, and the like);
aromatic acyl (e.g. benzoyl, toluoyl, naphthoyl, fluorenylcarbonyl and the like);
lower alkoxycarbonyl (e.g. methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl, isopropoxycarbonyl, butoxycarbonyl, isobutoxycarbonyl, t-butoxycarbonyl, pentyloxycarbonyl, hexyloxycarbonyl, and the like), and the like;
ar(lower)alkoxycarbonyl in which the aryl portion is optionally substituted with one or more suitable substituent(s) (e.g. benzyloxycarbonyl, bromobenzyloxycarbonyl and the like);
lower alkylsulfonyl (e.g. methylsulfonyl, ethylsulfonyl, and the like);
lower alkoxysulfonyl (e.g. methoxysulfonyl, ethoxysulfonyl, and the like);
ar(lower)alkanoyl (e.g. phenylacetyl, phenylpropanoyl, phenylbutanoyl, phenylisobutanoyl, phenylpentanoyl, phenylhexanoyl, naphthylacetyl, naphthylpropanoyl, naphthylbutanoyl, naphthylisobutanoyl, naphthylpentanoyl, naphthylhexanoyl, and the like);
ar(lower)alkenoyl such as ar(C_3-C_6)alkenoyl (e.g. phenylpropenoyl, phenylbutenoyl, phenylmethacryloyl, phenylpentenoyl, phenylhexenoyl, naphthylpropenoyl, naphthylbutenoyl, naphthylmethacryloyl, naphthylpentenoyl, naphthylhexenoyl, and the like); and the like];
lower alkenyl (e.g. vinyl, allyl, and the like), preferably allyl;
tetrahydropyranyl; and the like.

Suitable "amino protective group" may include:
acyl as exemplified for the hydroxy protective group;
ar(lower)alkyl in which the aryl portion is optionally

substituted with one or more suitable substituent(s) (e.g. benzyl, p-methoxybenzyl, o(or p)-nitrobenzyl, phenethyl, trityl, benzhydryl, bis(methoxyphenyl)methyl, m,p-dimethoxybenzyl, 4-hydroxy-3,5-di-t-butylbenzyl, and the like);
[5-(lower)alkyl-2-oxo-1,3-dioxol-4-yl](lower)alkyl (e.g. (5-methyl-2-oxo-1,3-dioxol-4-yl)methyl, (5-ethyl-2-oxo-1,3-dioxol-4-yl)methyl, (5-propyl-2-oxo-1,3-dioxol-4-yl)methyl, and the like), and the like; and the like.

Suitable "acyl" for the present invention may be illustrated as follows:
aliphatic acyl such as alkanoyl (e.g., formyl, acetyl, propanoyl, butanoyl, 2-methylpropanoyl, pentanoyl, pivaloyl, 2,2-dimethylpropanoyl, hexanoyl, heptanoyl, octanoyl, nonanoyl, decanoyl, undecanoyl, dodecanoyl, tridecanoyl, tetradecanoyl, pentadecanoyl, hexadecanoyl, heptadecanoyl, octadecanoyl, nonadecanoyl, icosanoyl, and the like);
alkoxycarbonyl (e.g., methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl, isopropoxycarbonyl, butoxycarbonyl, t-butoxycarbonyl, pentyloxycarbonyl, heptyloxycarbonyl, and the like);
alkylsulfonyl (e.g., methylsulfonyl, ethylsulfonyl, and the like);
alkoxysulfonyl (e.g., methoxysulfonyl, ethoxysulfonyl, and the like); and the like;
aromatic acyl such as aroyl (e.g., benzoyl, toluoyl, naphthoyl, fluorenylcarbonyl, and the like);
ar(lower)alkanoyl such as phenyl(lower)alkanoyl (e.g., phenylacetyl, phenylpropanoyl, phenylbutanoyl, phenylisobutanoyl, phenylpentanoyl, phenylhexanoyl, and the like),
naphthyl(lower)alkanoyl (e.g., naphthylacetyl, naphthylpropanoyl, naphthylbutanoyl, and the like), and the like;
ar(lower)alkenoyl such as ar(C_3-C_6)alkenoyl (e.g., phenylpropenoyl, phenylbutenoyl, phenylmethacryloyl, phenylpentenoyl, phenylhexenoyl, and the like),
naphthyl(C_3-C_6)alkenoyl (e.g., naphthylpropenoyl, naphthylbutenoyl, naphthylmethacryloyl, naphthylpentenoyl, naphthylhexenoyl, and the like), and the like;
ar(lower)alkoxycarbonyl such as phenyl(lower)alkoxycarbonyl (e.g., benzyloxycarbonyl, and the like), fluorenyl(lower)alkoxycarbonyl

(e.g., fluorenylmethyloxycarbonyl, and the like), and the like;
aryloxycarbonyl (e.g., phenoxycarbonyl, naphthyloxycarbonyl, and the like);
aryloxy(lower)alkanoyl (e.g., phenoxyacetyl, phenoxypropionyl, and the like);
arylcarbamoyl (e.g., phenylcarbamoyl and the like);
arylthiocarbamoyl (e.g., phenylthiocarbamoyl and the like);
arylglyoxyloyl (e.g., phenylglyoxyloyl, naphthylglyoxyloyl, and the like);
arylsulfonyl in which the aryl portion is optionally substituted with one or more suitable substituent(s) (e.g., phenylsulfonyl, p-tolylsulfonyl, and the like);
heterocyclic acyl (e.g. heterocycliccarbonyl and the like);
heterocyclic(lower)alkanoyl (e.g., heterocyclicacetyl, heterocyclicpropanoyl, heterocyclicbutanoyl, heterocyclicpentanoyl, heterocyclichexanoyl, and the like);
heterocyclic(lower)alkenoyl (e.g., heterocyclicpropenoyl, heterocyclicbutenoyl, heterocyclicpentenoyl, heterocyclichexenoyl, and the like); heterocyclicglyoxyloyl; and the like.

Suitable "heterocyclic" moiety in the terms "heterocycliccarbonyl", "heterocyclic(lower)alkanoyl", heterocyclic(lower)alkenoyl" and "heterocyclicglyoxyloyl" is the same as the above-mentioned "heterocyclic" for the "heterocyclic(lower)alkyl" for R^2.

Any "resin" known in the field of peptide synthesis may be used for the synthesis of the compound [I] of the present invention. Suitable example of the "resin" for the synthesis of the compound [I] includes 2-chlorotrityl resin and the like.

When the compound [I] has stereoisomers, such isomers are also encompassed in the present invention.

The compound [I] may form a salt, which is also encompassed in the present invention. For example, when a basic group such as an amino group is present in a molecule, the salt is exemplified by an acid addition salt (e.g. salt with an inorganic acid such as hydrochloric acid, hydrobromic acid, sulfuric acid, and the like, salt with an organic acid such as methanesulfonic acid, fumaric acid, maleic acid, mandelic acid, citric acid, salicylic acid, and the like) is exemplified, and when an acidic group such as carboxyl group is present, a basic salt (e.g. salt with a

metal such as sodium, potassium, calcium, magnesium, aluminium, and the like, a salt with amino acid such as lysine, and the like), and the like.

In addition, solvates of the compound [I] such as hydrate, ethanolate, and the like, are also encompassed in the present invention.

Hereinafter the reactions in each Preparations and Examples for preparing the cyclic tetrapeptide compound [I] of the present invention are explained in more detail. The invention should not be restricted by the following Preparations and Examples in any way.

<u>Preparation A</u>

<u>Preparation A-1</u>

The compound (a-2) can be prepared by protecting the carboxyl group of the compound (a-1).

Suitable protective agent for the reaction may be, for example, benzylhalide (e.g. benzylbromide and the like), methyl iodide, ethyl iodide, substituted benzyl halide, and the like.

The reaction may be carried out in the presence of a base (e.g. cesium carbonate, potassium carbonate, sodium carbonate, sodium hydrogen carbonate, triethylamine, 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), pyridine, and the like).

The reaction may be carried out in a conventional solvent which does not adversely influence the reaction (e.g. N,N-dimethylformamide, N-methylpyrrolidone, tetrahydrofuran, dimethylsulfoxide, and the like).

The reaction temperature is not critical and the reaction is usually carried out from under cooling to heating.

This Preparation is exemplified by Preparation 13 and the like.

<u>Preparation A-2</u>

The compound (a-3) can be prepared by 1) deprotecting the amino group of the compound (a-2) and 2) reacting the compound (a-2) with the compound (d-1).

1)Deprotection of the amino group of the compound (a-2)

Suitable deprotective agent for the reaction may be, for example, hydrogen chloride in suitable solvents (such as ethyl acetate, 1,4-dioxane, methanol, ethanol, and the like), trifluoroacetic acid, N,N-diethylamine, and the like. The

deprotection may also be conducted with a hydrogenolysis catalyst (e.g. palladium on carbon (Pd-C), palladium hydroxide on carbon, and the like) under hydrogen atmosphere. Specifically, when the carboxyl protective group of the compound (a-2) is t-butyl (e.g. Compound (47)) and the like, the reaction is carried out in the presence of the above-mentioned hydrogenolysis catalyst under hydrogen atmosphere.

The reaction may be carried out in a conventional solvent which does not adversely influence the reaction (e.g. ethyl acetate, dioxane, dichloromethane, acetonitrile, methanol, ethanol, tetrahydrofuran, acetic acid, and the like). Specifically, when trifluoroacetic acid is used as a deprotective agent, the reaction is generally carried out in dichloromethane or without solvent (neat).

The temperature of the reaction is not critical and the reaction is usually carried out from under cooling to heating under the pressure of 1-5 atm.

Alternatively, the compound (a-2) in which the amino group is not protected, may be obtained by directly protecting the carboxyl group of D-proline, in substantially the same manner as Preparation A-1.

2) Reaction of the compound (a-2) with the compound (d-1)

The reaction may be carried out in the presence of carbodiimide [e.g. 1-ethyl-3-(3'-N,N-dimethylaminopropyl)-carbodiimide (EDC) or hydrochrolide thereof, dicyclohexylcarbodiimide (DCC), and the like], benzotriazol-1-yloxy-tris-pyrrolidinophosphonium hexafluorophosphate (PyBOP®), benzotriazol-1-yloxy-tris-(dimethylamino)phosphonium hexafluoro phosphate (BOP), bromo-tris-pyrrolidinophosphonium hexafluorophosphate (PyBroP®), 1,1'-carbonyldiimidazol (CDI), diphenylphosphoryl azide (DPPA), 1-hydroxybenzotriazole (HOBT), benzotriazol-1-yloxy-tris-(dimethylamino)phosphonium-hexafluorophosphate (HATU), 2-(1H-benzotriazol-1-yl)-1,1,3,3-tetramethyluromium tetrafluoroborate (TBTU), 2-(1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HBTU), and the like, and a base [e.g. Hünig base (e.g. N,N-diisopropylethylamine, triethylamine, and the like), and the like], and the like.

The reaction may be carried out in a conventional solvent

which does not adversely influence the reaction (e.g. dichloromethane, N,N-dimethylformamide, and the like).

The temperature of the reaction is not critical and the reaction is usually carried out from under cooling to heating.

This Preparation is exemplified by Preparation 14 and the like.

Preparation A-3

The compound (a-4) can be prepared by 1) deprotecting the amino group of the compound (a-3) and 2) reacting the compound (a-3) with the compound (d-2).

1) Deprotection of the amino group of the compound (a-3)

The reaction may be carried out in substantially the same manner as described above for the deprotection of the amino group of the compound (a-2) in the Preparation A-2. Specifically, when the amino protective group is fluorenylmethyloxycarbonyl (Fmoc), a base such as N,N-diethylamine, piperidine, morpholine, dicyclohexylamine, 4-dimethylaminopyridine, N,N-diisopropylethyl amine and the like is used as a deprotective agent, and the reaction is generally carried out in a solvent such as N,N-dimethylformamide, acetonitrile, dichloromethane, and the like, or without solvent (neat).

2) Reaction of the compound (a-3) with the compound (d-2)

The reaction may be carried out in substantially the same manner as described above for the reaction of the compound (a-2) with the compound (d-1) in the Preparation A-2.

This Preparation is exemplified by Preparation 15 and the like.

Preparation A-4

The compound (a-5) can be prepared by 1) deprotecting the amino group of the compound (a-4) and 2) reacting the compound (a-4) with the compound (d-3).

1) Deprotection of the amino group of the compound (a-4).

The reaction may be carried out in substantially the same manner as described above for the deprotection of the amino group of the compound (a-2) in the Preparation A-2.

2) Reaction of the compound (a-4) with the compound (d-3)

This reaction may be carried out in substantially the same manner as described above for the reaction of the compound (a-2) with the compound (d-1) in the Preparation A-2.

This Preparation is exemplified by Preparation 16 and the like.

Preparation A-5

The compound (a-6) can be prepared by deprotecting the carboxyl group of the compound (a-5).

The reaction may be carried out using a catalyst (e.g. Pearlman catalyst ($Pd(OH)_2$-C), palladium on carbon (Pd-C), and the like) under hydrogen atmosphere. The reaction may also be carried out using an alkali (e.g. sodium hydroxide, potassium hydroxide, lithium hydroxide, and the like).

The reaction may be carried out in a conventional solvent which does not adversely influence the reaction (e.g. methanol, ethanol, ethyl acetate, 1,4-dioxane, tetrahydrofuran, and the like).

The temperature of the reaction is not critical and the reaction is usually carried out from under cooling to heating.

This reaction is exemplified by Preparation 17 and the like.

Preparation A-6

The compound [II] may be prepared by deprotecting the amino group of the compound (a-6).

The reaction may be carried out in substantially the same manner as described for the deprotection of the amino group of the compound (a-2) in the Preparation A-2.

This Preparation is exemplified by Preparation 18 and the like.

Preparation A-5+6

Alternatively, when the carboxy protective group is t-butyl, the deprotection of carboxyl group and amino group of the compound (a-5) may be conducted simultaneously to give the Compound [II].

In this case, suitable deprotective agent for this reaction may be, for example, trifluoroacetic acid and the like.

The reaction may be carried out in a conventional solvent which does not adversely influence the reaction (e.g. dichloromethane, and the like).

The temperature of the reaction is not critical and the reaction is usually carried out from under cooling to heating.

This reaction is exemplified by Preparation 53, 57 and the like.

The compound [II] as obtained above is used in the Preparation C.

Preparation B

Preparation B-1

The compound (b-2) may be prepared by reacting the compound (b-1) with the compound (d-4).

The reaction may be carried out in the presence of a base (e.g. diisopropylethylamine) in suitable solvent (e.g. dichloromethane, ethyl acetate, 1,4-dioxane, methanol, ethanol, and the like).

The reaction may be carried out in a conventional solvent which does not adversely influence the reaction (e.g. dichloromethane and the like).

The temperature of the reaction is not critical and the reaction is usually carried out from under cooling to heating.

This Preparation is exemplified by Preparation 65 and the like.

Preparation B-2

The compound (b-3) may be prepared by 1) deprotecting the amino group of the compound (b-2), and 2) reacting the compound (b-2) with the compound (d-1).

1) Deprotection of the amino group of the compound (b-2)

The reaction may be carried out in substantially the same manner as described above for the deprotection of the amino group of the compound (a-2) in the Preparation A-2.

2) Reaction of the compound (b-2) with the compound (d-1)

The reaction may be carried out in the presence of PyBOP®, HATU, and the like, and a base (e.g. Hünig base (e.g. N,N-diisopropylethylamine and the like) and the like).

The reaction may be carried out in a conventional solvent which does not adversely influence the reaction (e.g. N,N-dimethylformamide and the like).

The temperature of the reaction is not critical and the reaction is usually carried out from under cooling to heating.

This Preparation is exemplified by Preparation 66 and the like.

Preparation B-3

The compound (b-4) may be prepared by 1) deprotecting the amino group of the compound (b-3), and 2) reacting the compound

(b-3) with the compound (d-2).

1) Deprotection of the amino group of the compound (b-3)

The reaction may be carried out in substantially the same manner as described above for the deprotection of the amino group of the compound (a-2) in the Preparation A-2.

2) Reaction of the compound (b-3) with the compound (d-2)

The reaction may be carried out in substantially the same manner as in Preparation B-2.

This Preparation is exemplified by Preparation 67 and the like.

<u>Preparation B-4</u>

The compound (b-5) may be prepared by 1) deprotecting the amino group of the compound (b-4), and 2) reacting the compound (b-4) with the compound (d-3).

1) Deprotection of the amino group of the compound (b-4)

The reaction may be carried out in substantially the same manner as described above for the deprotection of the amino group of the compound (a-2) in the Preparation A-2.

2) Reaction of the compound (b-4) with the compound (d-3)

The reaction may be carried out in the presence of PyBOP®, HATU, and the like, and a base (e.g. Hünig base (e.g. N,N-diisopropylethylamine and the like) and the like).

The reaction may be carried out in a conventional solvent which does not adversely influence the reaction (e.g. dichloromethane, N,N-dimethylformamide, and the like).

The temperature of the reaction is not critical and the reaction is usually carried out from under cooling to heating.

This Preparation is exemplified by Preparation 68 and the like.

<u>Preparation B-5</u>

The compound [II] may be prepared by deprotecting the amino group and the carboxyl group attached to the resin unit of the compound (b-5).

The reaction may be carried out in the presence of an acid (e.g. trifluoroacetic acid and the like).

The reaction may be carried out in a conventional solvent which does not adversely influence the reaction (e.g. dichloromethane and the like).

The temperature of the reaction is not critical and the

reaction is usually carried out from under cooling to heating.

This Preparation is exemplified by Preparation 69 and the like.

The compound [II] is used in the Preparation C.

<u>Preparation C</u>

<u>Preparation C-1</u>

The compound [III] may be prepared by cyclizing the compound [II].

The reaction may be carried out in the presence of a reagent (e.g. HATU, BOP, PyBOP®, TBTU, HOBT, and the like), and a base (e.g. dimethylaminopyridine, triethylamine, N,N-diisopropylethylamine, and the like).

The reaction may be carried out in a conventional solvent which does not adversely influence the reaction (e.g. N,N-dimethylformamide, methylene chloride, and the like).

The temperature of the reaction is not critical and the reaction is usually carried out from under cooling to heating.

This Preparation is exemplified by Preparation 76 and the like.

<u>Preparation C-2</u>

The compound [IV] may be prepared by deprotecting the hydroxyl group of the compound [III].

The reaction may be carried out in the presence of a base (e.g. sodium hydroxide, potassium hydroxide, lithium hydroxide, sodium methoxide, and the like).

The reaction may be carried out in a conventional solvent which does not adversely influence the reaction (e.g. methanol, ethanol, 1,4-dioxane, tetrahydrofuran, and the like).

The temperature of the reaction is not critical and the reaction is usually carried out from under cooling to heating.

This Preparation is exemplified by Preparation 77 and the like.

<u>Preparation C-3</u>

The compound [V] may be prepared by oxidation of the compound [IV].

Suitable oxidizing agent in the reaction may be, for example, Dess-Martin periodinane (i.e. 1,1,1-triacetoxy-1,1-dihydro-1,2-benziodoxol-3(1H)-one), and the like.

The reaction may be carried out in a conventional solvent

which does not adversely influence the reaction (e.g. dichloromethane, dimethylsulfoxide, and the like).

The temperature of the reaction is not critical and the reaction is usually carried out from under cooling to heating.

This Preparation is exemplified by Preparation 78 and the like.

The compound [V] is used in the Preparation of the compound [I] of the present invention.

Preparation of the compound [I] of the present invention

Preparation of the compound [I-1]

The compound [I-1] may be prepared by reacting the compound [V] with the compound (d-5).

Suitable compound (d-5) for the reaction may be, for example, dimethyl (3R)-tert-butyldimethylsilyloxy-2-oxobutylphosphonate, dimethyl (3S)-tert-butyldimethylsilyloxy-2-oxobutylphosphonate, dimethyl (3R)-tert-butyldimethylsilyloxy-2-oxoheptylphosphonate, dimethyl 3-fluoro-2-oxopropylphosphonate, and the like.

The reaction may be carried out in the presence of a base (e.g. barium hydroxide octahydrate, barium hydroxide monohydrate, sodium hydroxide, potassium tert-butoxide, cesium carbonate, and the like).

The reaction may be carried out in a conventional solvent which does not adversely influence the reaction (e.g. tetrahydrofuran, tetrahydrofuran-water mixture, N,N-dimethylformamide, dimethylsulfoxide, acetonitrile, ethanol, 2-propanol, and the like).

The temperature of the reaction is not critical and the reactions are usually carried out from under cooling to heating.

The reaction may also be carried out in the presence of an organic base (e.g. Hünig base, DBU, and the like) and a lithium salt (e.g. lithium chloride, lithium bromide, lithium iodide, and the like), in a suitable solvent (e.g. acetonitrile, dimethylformamide, and the like) [Horner-Wadsworth-Emmons reaction].

The temperature of the reaction is not critical and the reactions are usually carried out from under cooling to heating.

The Preparation of the compound [I-1] is exemplified by Example 1 and the like.

Preparation of the compound [I-2]

The compound [I-2] may be prepared by hydrogenation of alkenylene of the compound [I-1'].

Suitable catalyst for the hydrogenation may be, for example, palladium-$BaSO_4$ (Pd-$BaSO_4$), palladium on carbon (Pd-C), $Pd(OH)_2$ on carbon, and the like.

The reaction may be carried out in a conventional solvent which does not adversely influence the reaction (e.g. methanol, ethyl acetate, ethanol, 1,4-dioxane, and the like).

The temperature of the reaction is not critical and the reaction is usually carried out from under cooling to heating.

The Preparation of the compound [I-2] is exemplified by Example 3 and the like.

Preparation of the compound [I-3]

The compound [I-3] may be prepared by deprotecting the hydroxyl group of the compound [I-1] or [I-2].

Suitable agent for the reaction may be, for example, tetrabutylammonium fluoride, pyridinium poly(hydrogen fluoride), hydrogen fluoride, cesium fluoride, potassium fluoride, and the like.

The reaction may be carried out in a conventional solvent which does not adversely influence the reaction (e.g. tetrahydrofuran, N,N-dimethylformamide, pyridine, and the like). Optionally, the reaction may be carried out in the presence of a catalyst (e.g. Pearlman catalyst ($Pd(OH)_2$-C), palladium on carbon (Pd-C), and the like) under hydrogen atmosphere.

The temperature of the reaction is not critical and the reaction is usually carried out from under cooling to heating.

The Preparation of the compound [I-3] is exemplified by Example 6 and the like.

To determine absolute configuration of the hydroxyl group of the compound [I-3] and to estimate optical purity of the isomer of the compound [I-3], the compound [I-3] is reacted with a reagent such as (R)-(-)-α-methoxy-α-trifluoromethyl-α-phenylacetyl chloride, (S)-(+)-α-methoxy-α-trifluoromethyl-α-phenylacetyl chloride, and the like.

The reaction may be carried out in a conventional solvent which does not adversely influence the reaction (e.g. pyridine, methylene chloride, and the like).

The temperature of the reaction is not critical and the reaction is usually carried out from under cooling to heating.

This reaction is exemplified by Example 53.

Preparation of the compound [I-4]

The compound [I-4] may be prepared by reacting the compound [I-3'] with sodium periodate.

The reaction may be carried out in a conventional solvent which does not adversely influence the reaction (e.g. water, methanol, and the like).

The temperature of the reaction is not critical and the reaction is usually carried out from under cooling to heating.

The Preparation of the compound [I-4] is exemplified by Example 139 and the like.

Preparation of the compound [I-5]

The compound [I-5] may be prepared by reacting the compound [I-4] with the compound (d-6).

Suitable agent for the reaction may be, for example, carbodiimide [e.g. 1-ethyl-3-(3'-N,N-dimethylaminopropyl)-carbodiimide (EDC) or hydrochrolide thereof, dicyclohexylcarbodiimide (DCC), and the like], benzotriazol-1-yloxy-tris-pyrrolidinophosphonium hexafluorophosphate (PyBOP®), benzotriazol-1-yloxy-tris-(dimethylamino)phosphonium hexafluoro phosphate (BOP), bromo-tris-pyrrolidinophosphonium hexafluorophosphate (PyBroP®), 1,1'-carbonyldiimidazol (CDI), diphenylphosphoryl azide (DPPA), 1-hydroxybenzotriazole (HOBT), benzotriazol-1-yloxy-tris-(dimethylamino)phosphonium-hexafluorophosphate (HATU), 2-(1H-benzotriazol-1-yl)-1,1,3,3-tetramethyluromium tetrafluoroborate (TBTU), 2-(1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HBTU) and the like.

The reaction may be carried out in a conventional solvent which does not adversely influence the reaction (e.g. dichloromethane, N,N-dimethylformamide and the like).

The temperature of the reaction is not critical and the reaction is usually carried out from under cooling to heating.

The Preparation of the compound [I-5] is exemplified by Example 141 and the like.

Preparation of the compound [I-6]

The compound [I-6] may be prepared by reacting the compound

[I-5] with Grignard's agent [e.g. alkylmagnesium halide ($R^{11}MgQ$)]. Suitable alkylmagnesium halide for the reaction may be, for example, methyl magnesium bromide, ethyl magnesium bromide, phenyl magnesium bromide, benzyl magnesium bromide and the like.

The reaction may be carried out in a conventional solvent which does not adversely influence the reaction (e.g. tetrahydrofuran, diethylether and the like).

The temperature of the reaction is, for example, -78°C to 0°C.

The Preparation of the compound [I-6] is exemplified by Example 143 and the like.

Preparation of the compound [I-7]

The compound [I-7] may be prepared by reducing the compound [I-1] with a reductant.

Suitable reductant for the reaction may be, for example, sodium borohydride, lithium aluminum hydride, diisobutylalminum hydride, sodium cyanoborohydride, sodium triacetoxyborohydride and the like.

The reaction may be carried out in a conventional solvent which does not adversely influence the reaction (e.g. methanol, ethanol, tetrahydrofuran, dioxane, 2-propanol and the like).

The temperature of the reaction is not critical and the reaction is usually carried out from under cooling to heating.

The Preparation of the compound [I-7] is exemplified by Example 147 and the like.

Preparation of the compound [I-8]

The compound [I-8] may be prepared by fluoridation of a hydroxyl group of the compound [I-3'] with diethylaminosulfurtrifluoride.

The reaction may be carried out in a conventional solvent which does not adversely influence the reaction (e.g. dichloromethane, acetonitrile, acetic acid, chloroform, tetrahydrofuran, 2-propanol and the like).

The temperature of the reaction is not critical and the reaction is usually carried out from under cooling to heating.

The Preparation of the compound [I-8] is exemplified by Example 148 and the like.

Preparation of the compound [I-9]

The compound [I-9] may be prepared by reacting the compound

[I-5] with alkyllithium ($R^{12}Li$).

Suitable alkyllithium for the reaction may be, for example, n-butyllithium, methyllithium ethyllithium, isopropyllithium, iso-butyllithium, tert-butyllithium, n-hexyllithium, phenyllithium, vinyllithium and the like.

The reaction may be carried out in a conventional solvent which does not adversely influence the reaction (e.g. tetrahydrofuran, diethyl ether, cyclohexane and the like).

The temperature of the reaction is, for example, -78°C to 0°C.

The Preparation of the compound [I-9] is exemplified by Example 149 and the like.

Preparation of the compound [I-10]

The compound [I-10] may be prepared by reacting the compound [I-1''] with a secondary amine ($R^{13}R^{14}NH$).

Suitable secondary amine for this reaction may be, for example, piperidine, morpholine, dicyclohexylamine, diethylamine and the like.

The reaction may be carried out in a conventional solvent which does not adversely influence the reaction (e.g. N,N-dimethylformamide, and the like).

The temperature of the reaction is not critical and the reaction is usually carried out from under cooling to heating.

The Preparation of the compound [I-10] is exemplified by Example 150 and the like.

Preparation of the compound [I-11]

The compound [I-11] may be prepared by reacting the compound [I-10] with methanesulfonyl chloride.

The reaction may be carried out in a conventional solvent which does not adversely influence the reaction (e.g. pyridine, dichloromethane, and the like).

The temperature of the reaction is, for example, 0°C to room temperature.

The Preparation of the compound [I-11] is exemplified by Example 151 and the like.

Preparation of the compound [I-12]

The compound [I-12] may be prepared by reacting the compound [I-11] with acetic anhydride in the presence of a catalytic amount of 4-(dimethylamino)pyridine.

The reaction may be carried out in a conventional solvent which does not adversely influence the reaction (e.g. pyridine, dichloromethane and the like).

The temperature of the reaction is not critical and the reaction is usually carried out from under cooling to heating.

The Preparation of the compound [I-12] is exemplified by Example 153 and the like.

Test Method

In order to show the usefulness of the compound [I] of the invention, the pharmacological test result of the representative compounds of the present invention is shown in the following.

Test 1: Determination of histone deacetylase inhibitor activity

The partial purification of human histone deacetylase, the preparation of [^{3}H] acetyl histones, and the assay for histone deacetylase activity were performed basically according to the method as proposed by Yoshida et al. as follows.

Partial purification of human histone deacetylase

The human histone deacetylase was partially purified from human T cell leukemia Jurkat cells. Jurkat cells (5×10^8 cells) were suspended in 40 ml of the HDA buffer consisting of 15 mM potassium phosphate, pH 7.5, 5% glycerol and 0.2 mM EDTA. After homogenization, nuclei were collected by centrifugation (35,000 x g, 10 min) and homogenized in 20 ml of the same buffer supplemented with 1 M $(NH_4)_2SO_4$. The viscous homogenate was sonicated and clarified by centrifugation (35,000 x g, 10 min), and the deacetylase was precipitated by raising the concentration of $(NH_4)_2SO_4$ to 3.5 M. The precipitated protein was dissolved in 10 ml of the HDA buffer and dialyzed against 4 liters of the same buffer. The dialyzate was then loaded onto a DEAE-cellulose (Whatman DE52) column (25 x 85 mm) equilibrated with the same buffer and eluted with 300 ml of a linear gradient (0-0.6 M) of NaCl. A single peak of histone deacetylase activity appeared between 0.3 and 0.4 M NaCl.

Preparation of [^{3}H] acetyl histone

To obtain [^{3}H] acetyl-labeled histone as the substrate for the histone deacetylase assay, 1×10^8 cells of Jurkat in 20 ml of RPMI-1640 medium (supplemented with 10% FBS, penicillin (50 units/ml) and streptomycin (50μg/ml)) were incubated with 300 MBq [^{3}H] sodium acetate in the presence of 5 mM sodium butyrate for 30

minutes in 5% CO_2-95% air atmosphere at 37°C in a 75 cm^2 flask, harvested into a centrifuge tube (50 ml), collected by centrifugation at 1000 rpm for 10 minutes, and washed once with phosphate-buffered saline. The washed cells were suspended in 15 ml of ice-cold lysis buffer (10 mM Tris-HCl, 50 mM sodium bisulfite, 1% Triton X-100, 10 mM $MgCl_2$, 8.6% sucrose, pH 6.5). After Dounce homogenization (30 stroke), the nuclei were collected by centrifugation at 1000 rpm for 10 minutes, washed 3 times with 15 ml of the lysis buffer, and once with 15 ml of ice-cooled washing buffer (10 mM Tris-HCl, 13 mM EDTA, pH 7.4) successively. The pellet was suspended in 6 ml of ice-cooled water using a mixer, and 68μl of H_2SO_4 was added to the suspension to give a concentration of 0.4 N. After incubation at 4°C for 1 hour, the suspension was centrifuged for 5 minutes at 15,000 rpm, and the supernatant was taken and mixed with 60 ml of acetone. After overnight incubation at -20°C, the coagulated material was collected by microcentrifugation, air-dried, and stored at -80°C.

Assay for histone deacetylase activity

For the standard assay, 10 μl of [^{3}H] acetyl-labeled histones were added to 90μl of the enzyme fraction, and the mixture was incubated at 25°C for 30 minutes. The reaction was stopped by addition of 10 μl of HCl. The released [^{3}H] acetic acid was extracted with 1 ml of ethyl acetate, and 0.9 ml of the solvent layer was taken into 10 ml of toluene scintillation solution for determination of radioactivity.

Test 2: Determination of T-cell growth inhibitor activity

The T lymphocyte blastogenesis test was performed in microtiter plates with each well containing 1.5 x 10^5 splenic cells of Lewis rats in 0.1 ml RPMI-1640 medium supplemented with 10% fetal bovine serum (FBS), 50 mM 2-mercaptoethanol, penicilln (100 units/ml) and streptomycin (100μg/ml), to which Concanavalin A (1μg/ml) was added. The cells were incubated at 37°C in a humidified atmosphere of 5% CO_2 for 72 hours. After the culture period, suppressive activities of the test compounds in T lymphocyte blastogenesis were quantified by AlamarBlue ™ Assay. The test samples were dissolved in DMSO and further diluted with RPMI-1640 medium and added to the culture. The activities of the test compounds were expressed as IC_{50}.

The results of those tests are shown in the Table 1.

Table 1: HDAC inhibitory activity and T-cell growth inhibitory activity of the compound of the present invention

Example	Test 1: HDAC inhibitory activity IC_{50} (nM)	Test 2: T-cell growth inhibitory activity IC_{50} (nM)
Compound E6	19	19
Compound E8	15	21
Compound E13	12	1.0
Compound E17	16	15
Compound E23	14	2.9
Compound E26	15	1.1
Compound E33	29	13
Compound E34	200	180
Compound E35	76	19
Compound E38	12	3.6
Compound E41	19	47
Compound E47	2000	34
Compound E48	74	23
Compound E49	1000	25
Compound E59	34	77
Compound E61	860	>1000

The pharmaceutical composition of the present invention comprising histone deacetylase inhibitor, such as the compound [I], is useful as a therapeutic or prophylactic agent for diseases caused by abnormal gene expression, such as inflammatory disorders, diabetes, diabetic complications, homozygous thalassemia, fibrosis, cirrhosis, acute promyelocytic leukaemia (APL), protozoal infection and the like. Further, it is useful as an antitumor agent or immunosuppressant, which prevents an organ transplant rejection and autoimmune diseases as exemplified below.

Rejection reactions by transplantation of organs or tissues such as the heart, kidney, liver, bone marrow, skin, cornea, lung, pancreas, small intestine, limb, muscle, nerve, intervertebral disc, trachea, myoblast, cartilage, and the like;

graft-versus-host reactions following bone marrow transplantation;

autoimmune diseases such as rheumatoid arthritis, systemic lupus erythematosus, Hashimoto's thyroiditis, multiple sclerosis, myasthenia gravis, type I diabetes, and the like;

and infections caused by pathogenic microorganisms (e.g. Aspergillus fumigatus, Fusarium oxysporum, Trichophyton asteroides, and the like).

Furthermore, pharmaceutical preparations of the histone deacetylase inhibitor, such as the compound [I], are useful for the therapy or prophylaxis of the following diseases.

Inflammatory or hyperproliferative skin diseases or cutaneous manifestations of immunologically-mediated diseases (e.g. psoriasis, atopic dermatitis, contact dermatitis, eczematoid dermatitis, seborrheic dermatitis, lichen planus, pemphigus, bullous pemphigoid, epidermolysis bullosa, urticaria, angioedema, vasculitides, erythema, dermal eosinophilia, lupus erythematosus, acne, and alopecia areata);

autoimmune diseases of the eye (e.g. keratoconjunctivitis, vernal conjunctivitis, uveitis associated with Behcet's disease, keratitis, herpetic keratitis, conical keratitis, corneal epithelial dystrophy, keratoleukoma, ocular premphigus, Mooren's ulcer, scleritis, Grave's ophthalmopathy, Vogt-Koyanagi-Harada syndrome, keratoconjunctivitis sicca (dry eye), phlyctenule, iridocyclitis, sarcoidosis, endocrine ophthalmopathy, and the like);

reversible obstructive airways diseases [asthma (e.g. bronchial asthma, allergic asthma, intrinsic asthma, extrinsic asthma, and dust asthma), particularly chronic or inveterate asthma (e.g. late asthma and airway hyper-responsiveness) bronchitis, and the like];

mucosal or vascular inflammations (e.g. gastric ulcer, ischemic or thrombotic vascular injury, ischemic bowel diseases, enteritis, necrotizing enterocolitis, intestinal damages associated with thermal burns, leukotriene B4-mediated diseases);

intestinal inflammations/allergies (e.g. coeliac diseases, proctitis, eosinophilic gastroenteritis, mastocytosis, Crohn's disease and ulcerative colitis);

food-related allergic diseases with symptomatic manifestation remote from the gastrointestinal tract (e.g. migrain, rhinitis and eczema);

renal diseases (e.g. intestitial nephritis, Goodpasture's syndrome, hemolytic uremic syndrome, and diabetic nephropathy);
nervous diseases (e.g. multiple myositis, Guillain-Barre syndrome, Meniere's disease, multiple neuritis, solitary neuritis, cerebral infarction, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis (ALS), and radiculopathy);
cerebral ischemic diseases (e.g., head injury, hemorrhage in brain (e.g., subarachnoid hemorrhage, intracerebral hemorrhage), cerebral thrombosis, cerebral embolism, cardiac arrest, stroke, transient ischemic attack (TIA), and hypertensive encephalopathy);
endocrine diseases (e.g. hyperthyroidism, and Basedow's disease);
hematic diseases (e.g. pure red cell aplasia, aplastic anemia, hypoplastic anemia, idiopathic thrombocytopenic purpura, autoimmune hemolytic anemia, agranulocytosis, pernicious anemia, megaloblastic anemia, and anerythroplasia);
bone diseases (e.g. osteoporosis);
respiratory diseases (e.g. sarcoidosis, pulmonary fibrosis, and idiopathic interstitial pneumonia);
skin diseases (e.g. dermatomyositis, leukoderma vulgaris, ichthyosis vulgaris, photosensitivity, and cutaneous T-cell lymphoma);
circulatory diseases (e.g. arteriosclerosis, atherosclerosis, aortitis syndrome, polyarteritis nodosa, and myocardosis);
collagen diseases (e.g. scleroderma, Wegener's granuloma, and Sjögren's syndrome);
adiposis;
eosinophilic fasciitis;
periodontal diseases (e.g. damage to gingiva, periodontium, alveolar bone or substantia ossea dentis);
nephrotic syndrome (e.g. glomerulonephritis);
male pattern alopecia, alopecia senile;
muscular dystrophy;
pyoderma and Sezary syndrome;
chromosome abnormality-associated diseases (e.g. Down's syndrome);
Addison's disease;
active oxygen-mediated diseases [e.g. organ injury (e.g. ischemic circulation disorders of organs (e.g. heart, liver, kidney,

digestive tract, and the like) associated with preservation, transplantation, or ischemic diseases (e.g. thrombosis, cardial infarction, and the like):
intestinal diseases (e.g. endotoxin shock, pseudomembranous colitis, and drug- or radiation-induced colitis):
renal diseases (e.g. ischemic acute renal insufficiency, chronic renal failure):
pulmonary diseases (e.g. toxicosis caused by pulmonary oxygen or drugs (e.g. paracort, bleomycin, and the like), lung cancer, and pulmonary emphysema):
ocular diseases (e.g. cataracta, iron-storage disease (siderosis bulbi), retinitis, pigmentosa, senile plaques, vitreous scarring, corneal alkali burn):
dermatitis (e.g. erythema multiforme, linear immunoglobulin A bullous dermatitis, cement dermatitis):
and other diseases (e.g. gingivitis, periodontitis, sepsis, pancreatitis, and diseases caused by environmental pollution (e.g. air pollution), aging, carcinogen, metastasis of carcinoma, and hypobaropathy)];
diseases caused by histamine release or leukotriene C4 release;
restenosis of coronary artery following angioplasty and prevention of postsurgical adhesions;
autoimmune diseases and inflammatory conditions (e.g., primary mucosal edema, autoimmune atrophic gastritis, premature menopause, male sterility, juvenile diabetes mellitus, pemphigus vulgaris, pemphigoid, sympathetic ophthalmitis, lens-induced uveitis, idiopathic leukopenia, active chronic hepatitis, idiopathic cirrhosis, discoid lupus erythematosus, autoimmune orchitis, arthritis (e.g. arthritis deformans), or polychondritis);
Human Immunodeficiency Virus (HIV) infection, AIDS;
allergic conjunctivitis;
hypertrophic cicatrix and keloid due to trauma, burn, or surgery.

Therefore, the pharmaceutical composition of the present invention is useful for the therapy and prophylaxis of liver diseases [e.g. immunogenic diseases (e.g. chronic autoimmune liver diseases such as autoimmune hepatic diseases, primary biliary cirrhosis or sclerosing cholangitis), partial liver resection, acute liver necrosis (e.g. necrosis caused by toxins, viral hepatitis, shock, or anoxia), hepatitis B, non-A non-B

hepatitis, hepatocirrhosis, and hepatic failure (e.g. fulminant hepatitis, late-onset hepatitis and "acute-on-chronic" liver failure (acute liver failure on chronic liver diseases))].

The pharmaceutical composition of the present invention can be used in the form of pharmaceutical preparation, for example, in a solid, semisolid or liquid form, which contains the histone deacetylase inhibitor, such as the compound [I], as an active ingredient in admixture with an organic or inorganic carrier or excipient suitable for external, enteral or parenteral administrations. The active ingredient may be compounded, for example, with the usual non-toxic, pharmaceutically acceptable carriers for tablets, pellets, capsules, suppositories, solutions, emulsions, suspensions, injections, ointments, liniments, eye drops, lotion, gel, cream, and any other form suitable for use.

The carriers which can be used are water, glucose, lactose, gum acacia, gelatin, mannitol, starch paste, magnesium trisilicate, talc, corn starch, keratin, colloidal silica, potato starch, urea and other carriers suitable for use in manufacturing preparations, in a solid, semisolid, or liquid form, and in addition auxiliary, stabilizing, thickening, solubilizing and coloring agents and perfumes may be used.

For applying the composition to human, it is preferable to apply it by intravenous, intramuscular, topical or oral administration. While the dosage of therapeutically effective amount of the histone deacetylase inhibitor, such as the compound [I], varies from and also depends upon the age and condition of each individual patient to be treated, when an individual patient is to be treated, in the case of intravenous administration, a daily dose of 0.01-10 mg of the histone deacetylase inhibitor, such as the compound [I], per kg weight of human being, in the case of intramuscular administration, a daily dose of 0.1-10 mg of the histone deacetylase inhibitor, such as the compound of the formula [I], per kg weight of human being, and in the case of oral administration, a daily dose of 0.5-50 mg of the histone deacetylase inhibitor, such as the compound [I], per kg weight of human being, is generally given for treatment.

The following Preparations and Examples are given for the purpose of illustrating the present invention in more detail.

Preparation 1

To a stirred solution of 2(S)-(+)-amino-2-methylbutanoic acid monohydrate (15 g) in 1,4-dioxane (225 ml), a mixture of 1N sodium hydroxide aqueous solution (111 ml) and di-tert-butyl dicarbonate (24.2 g) was added at ambient temperature and the resulting mixture was stirred for 53 hours. Additional mixture of di-tert-butyl dicarbonate (24.2 g) and 1N sodium hydroxide aqueous solution (111 ml) was added at 8 hours, 24 hours and 48 hours after the start of the reaction. The mixture was diluted with diethyl ether (400 ml) and the organic phase was separated. The pH of the aqueous phase was adjusted to 1 with concentrated hydrochloric acid. The aqueous phase was extracted with ethyl acetate (500 ml) twice and the organic layers were combined, washed with brine (500 ml), dried over anhydrous sodium sulfate and concentrated in vacuo. The residual solid was treated with hexane (100 ml) and the resulting suspension was stirred in an ice bath for one hour. The precipitate was filtered and washed with cold hexane to afford 2(S)-N-tert-butoxycarbonylamino-2-methylbutanoic acid (21.71 g, hereinafter Compound (1)) as a white amorphous solid.

^{1}H-NMR (300MHz, DMSO-d_6, δ): 6.82 (1H, brs), 1.61-1.82 (2H, m), 1.36 (9H, s), 0.75 (3H, t, J=7.5Hz);

MASS (ES-): m/e 216.17.

Preparation 2

To a solution of (S)-2-amino-6-hydroxyhexanoic acid (2.0 g) and sodium hydrogen carbonate (2.28 g) in dioxane-water mixture (20 ml : 20 ml) was added di-tert-butyl dicarbonate (5.93 g) at room temperature. The resulting mixture was stirred at room temperature for 6 hours. The reaction mixture was diluted with water and washed with ether. The aqueous phase was adjusted to pH 2 with conc. hydrochloric acid and extracted with ethyl acetate. The organic layer was washed with water and brine, dried over anhydrous sodium sulfate and concentrated in vacuo to give 2(S)-N-tert-butoxycarbonylamino-6-hydroxyhexanoic acid as a solid.

^{1}H-NMR (300MHz, DMSO-d_6, δ): 1.18-1.45 (4H, m), 1.37 (9H, s), 1.45-1.70 (2H, m), 3.35 (2H, m), 3.75-3.88 (1H, m), 4.31-4.45 (1H, br), 7.06 (1H, d, J=7.5Hz);

MASS (ES-): m/e 246.15 (M-1).

Preparation 3

To a solution of 2(S)-N-tert butoxycarbonylamino-6-hydroxyhexanoic acid (3.36 g) in N,N-dimethylformamide (35 ml), cesium carbonate powder was added (2.21 g) at 0°C and stirred for 1.5 hours at room temperature. To the mixture, benzylbromide (1.66 ml) was added at 0°C and stirred for 1.5 hours. The reaction mixture was stirred for further 1.5 hours at room temperature. The reaction mixture was poured into water under ice-cooling and extracted with ethyl acetate. The organic layer was washed with water (3 times) and brine, dried over anhydrous sodium sulfate and concentrated in vacuo to give 2(S)-N-tert-butoxycarbonylamino-6-hydroxyhexanoic acid benzyl ester as a pale yellow crude oil.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.44 (9H, s), 1.48-1.90 (7H, m), 3.55-3.65 (2H, m), 4.30-4.41 (1H, m), 5.02-5.10 (1H, m), 5.10-5.25 (2H, m), 7.36 (5H, br.s);

MASS (ES-): m/e 338.23 (M+1).

Preparation 4

To a solution of 2(S)-N-tert-butoxycarbonylamino-6-hydroxyhexanoic acid benzyl ester (4.58 g) in pyridine (13 ml), benzoylchloride (2 g) was added at 0°C and stirred for 1.5 hours at room temperature. The reaction mixture was poured into cooled 1N hydrochloric acid (150 ml) and stirred for 10 minutes. The resulting mixture was extracted with ethyl acetate. The organic layer was washed with water, saturated sodium hydrogen carbonate, water and brine, dried over anhydrous sodium sulfate and concentrated in vacuo. The crude product was purified by column chromatography (eluting with ethyl acetate/hexane = 10/1 to 4/1 v/v) to give 2(S)-N-tert-butoxycarbonylamino-6-benzoyloxyhexanoic acid benzyl ester as a pale yellow oil.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.35-1.60 (2H, m), 1.43 (9H, s), 1.62-1.96 (4H, m), 4.26 (1H, t, J=6.0Hz), 4.30-4.42 (1H, m), 5.00-5.08 (1H, m), 5.08-5.22 (2H, m), 7.34 (5H, s), 7.39-7.46 (2H, m), 7.52-7.60 (1H, m), 7.98-8.05 (2H, m);

MASS (ES+): m/e 442.34.

Preparation 5

To a solution of 2(S)-N-tert-butoxycarbonylamino-6-benzoyloxyhexanoic acid benzyl ester (5.43 g) in methanol (55 ml), palladium hydroxide on charcoal catalyst (50 mg) was added. The air atmosphere was replaced with hydrogen (4 atm) and shaken for

3 hours. The resulting mixture was filtered through a pad of Celite®, and washed with methanol. The filtrate was concentrated in vacuo to give 6-benzoyloxy-2(S)-N-tert-butoxycarbonylamino-hexanoic acid (hereinafter Compound (5)) as a pale yellow oil.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.44 (9H, s), 1.47-2.05 (6H, m), 4.12-4.27 (1H, m), 4.44 (2H, t, J=6.0Hz), 5.00-5.12 (1H, m), 7.38-7.50 (2H, m), 7.50-7.62 (1H, m), 8.00-8.07 (2H, m);

MASS (ES+): m/e 352.20 (M+1).

Preparation 6

To a cooled suspension of N-tert-butoxycarbonylamino-6-methoxy-6-oxo-L-norleucine dicyclohexylamine salt (21.1 g) in N,N-dimethylformamide (210 ml) was added benzyl bromide (7.9 g), and the mixture was stirred at ambient temperature for 3 days. The mixture was evaporated in vacuo. The residue was diluted with ethyl acetate and the remaining solid was filtered off. The filtrate was washed with 10% aqueous citric acid solution, saturated sodium hydrogen carbonate solution and brine, dried over magnesium sulfate and evaporated in vacuo. The residue was purified by silica gel column chromatography (eluting with hexane/ethyl acetate = 4:1 to 2:1 v/v) to give N-tert-butoxycarbonyl-6-methoxy-6-oxo-L-norleucine benzyl ester (15.4 g) as a white solid.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.28 (3x3H, s), 1.59-1.75 (3H, m), 1.83 (1H, m), 2.31 (2H, m), 3.65 (3H, s), 4.35 (1H, m), 5.06 (1H, br-d, J=8Hz), 5.14 (1H, d, J=12Hz), 5.20 (1H, d, J=12Hz), 7.30-7.42 (5H, m);

MASS (ES+): m/e 366.

Preparation 7

To a stirred solution of N-tert-butoxycarbonyl-6-methoxy-6-oxo-L-norleucine benzyl ester (15.4 g) in acetonitrile (150ml) were added 4-dimethylaminopyridine (1.03 g) and di-tert-butyldicarbonate (14.7 g), and the mixture was stirred at ambient temperature for 1 day. The mixture was evaporated in vacuo. The residue was purified by silica gel column chromatography (eluting with hexane/ethyl acetate = 10:1 v/v) to give N,N-di-tert-butoxycarbonyl-6-methoxy-6-oxo-L-norleucine as a colorless oil (20.0 g).

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.45 (2x9H, s), 1.70 (2H, m), 1.96 (1H, m), 2.15 (1H, m), 2.36 (2H, m), 3.66 (3H, s), 4.90 (1H, dd, J=9

and 4.5Hz), 5.13 (1H, d, J=11Hz), 5.17 (1H, d, J=11Hz), 7.28-7.39 (5H, m);
MASS (ES+): m/e 488.

Preparation 8

To a cooled solution of N,N-di-tert-butoxycarbonyl-6-methoxy-6-oxo-L-norleucine (9.71 g) in diethyl ether (150 ml) was added dropwise 1M solution of diisobutylaluminium hydride in hexane (DIBAL) (23 ml) at -78°C. After 30 minutes DIBAL (24 ml) was added dropwise until the starting compound was disappeared. The reaction mixture was quenched by addition of water. After warming to 0°C with stirring, the mixture was filtered through a pad of Celite®. The solvent was evaporated and the residual solvent was removed azeotropically with toluene to give N,N-di-tert-butoxycarbonyl-6-oxo-L-norleucine benzyl ester as a pale yellow oil (8.94 g).

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.45 (2x9H, s), 1.70 (2H, m), 1.96 (1H, m), 2.14 (1H, m), 2.49 (2H, m), 4.90 (1H, m), 5.13 (1H, d, J=12Hz), 5.17 (1H, d, J=12Hz), 7.26-7.39 (5H, m), 9.76 (1H, t, J=1Hz);
MASS (ES-): m/e 435.

Preparation 9

To a stirred solution of dimethyl (3R)-3-benzyloxy-2-oxobutylphosphonate (1.08 g), lithium chloride (174 mg), and N,N-diisopropylethylamine (442 mg) in acetonitrile (10 ml) was added a solution of N,N-di-tert-butoxycarbonyl-6-oxo-L-norleucine benzyl ester (1.49 g) in acetonitrile (30 ml) at ambient temperature. The mixture was stirred at ambient temperature for 5 days. After evaporation of the solvent, the residue was diluted with water, and extracted with ethyl acetate. The extract was washed with brine, dried over magnesium sulfate, and the solvent was evaporated in vacuo. The residue was purified by silica gel column chromatography (eluting with hexane/ethyl acetate = 10:1 v/v) to give benzyl (2S,6E)-9-benzyloxy-2-di-tert-butoxycarbonylamino-8-oxodec-6-enoate as an oil (1.13 g).

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.35 (3H, d, J=7Hz), 1.38-1.62 (6H, m), 1.44 (2x9H, s), 1.95 (1H, m), 2.16 (1H, m), 2.28 (2H, m), 4.05 (1H, q, J=7Hz), 4.41 (1H, d, J=12Hz), 4.56 (1H, d, J=12Hz), 4.90 (1H, dd, J=10 and 5Hz), 5.12 (1H, d, J=12Hz), 5.16 (1H, d, J=12Hz), 6.51 (1H, d, J=15Hz), 7.02 (1H, dt, J=15 and 7Hz), 7.23-

7.40 (5H, m);
MASS (ES+): m/e 618 (M+Na).

Preparation 10

A solution of benzyl (2S,6E)-9-benzyloxy-2-di-tert-butoxycarbonylamino-8-oxodec-6-enoate (2.74 g) in ethyl acetate (30 ml) was hydrogenated in the presence of 10% palladium-carbon (300 mg) for 2 hours. The reaction mixture was filtered through a pad of Celite® and concentrated in vacuo to give (2S)-9-benzyloxy-2-di-tert-butoxycarbonylamino-8-oxodecanoic acid as an oil (2.27 g).

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.19-1.53 (6H, m), 1.33 (3H, d, J=7Hz), 1.50 (2x9H, s), 1.89 (1H, m), 2.07 (1H, m), 2.44-2.65 (2H, m), 3.92 (1H, q, J=7Hz), 4.48 (1H, d, J=12Hz), 4.54 (1H, d, J=12Hz), 4.89 (1H, dd, J=10 and 5Hz), 7.22-7.40 (5H, m);
MASS (ES-): m/e 506.

Preparation 11

To a solution of (2S)-9-benzyloxy-2-di-tert-butoxycarbonylamino-8-oxodecanoic acid (164 mg) in dioxane (2 ml) was added 4N-hydrogen chloride in dioxane (2 ml), and the mixture was stirred at ambient temperature for 3 hours. The solvent was evaporated in vacuo and the residual solvent was removed azeotropically with toluene to give (2S)-2-amino-9-benzyloxy-8-oxodecanoic acid hydrochloride as an amorphous (109 mg).

^{1}H-NMR (300MHz, DMSO-d_6, δ): 1.16-1.53 (6H, m), 1.23 (3H, d, J=7Hz), 1.76 (2H, m), 2.55 (2H, m), 3.86 (1H, t, J=5Hz), 3.99 (1H, q, J=7Hz), 4.46 (1H, d, J=12Hz), 4.51 (1H, d, J=12Hz), 7.26-7.41 (5H, m), 8.30 (2H, br);
MASS (ES+): m/e 308.

Preparation 12

To a stirred solution of (2S)-2-amino-9-benzyloxy-8-oxodecanoic acid hydrochloride (1.37 g) in dioxane (20 ml) were added 1N-sodium hydroxide (8.8 ml) and di-tert-butyldicarbonate (1.04 g) in dioxane, and the mixture was stirred at ambient temperature for 4 hours. The mixture was concentrated in vacuo. The residue was diluted with water and the mixture was washed with diethyl ether. The aqueous phase was acidified with 1N-hydrogen chloride, and extracted with ethyl acetate. The organic phase was washed with brine, dried over magnesium sulfate, and evaporated in vacuo to give (2S)-9-benzyloxy-2-tert-

butoxycarbonylamino-8-oxodecanoic acid (hereinafter Compound (12)) as a colorless oil (1.48 g).
^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.21-1.46 (4H, m), 1.33 (3H, d, J=7Hz), 1.52-1.74 (3H, m), 1.84 (1H, m), 2.55 (2H, m), 3.72 (1H, q, J=7Hz), 4.28 (1H, m), 4.49 (1H, d, J=12Hz), 4.55 (1H, d, J=12Hz), 4.97 (1H, br-d, J=8Hz), 7.21-7.40 (5H, m);
MASS (ES-): m/e 406.

Preparation 13

To a stirred solution of N-tert-butoxycarbonyl-(R)-proline (50 g) in N,N-dimethylformamide (250 ml), cesium carbonate (37.8 g) was added portionwise under ice-cooling in an ice bath. The ice bath was removed and the suspension was stirred at ambient temperature for 1.5 hours. To the suspension benzyl bromide (40.9 g) was added under ice-cooling and the mixture was stirred at ambient temperature for two and half an hour. To this mixture, water (250 ml) was added under ice-cooling and the mixture was extracted with ethyl acetate (1500 ml), and washed with water (250 ml, 3 times) and brine (250 ml). The organic layer was dried over anhydrous sodium sulfate, filtered and the filtrate was concentrated in vacuo to give crude Compound (13) (N-tert-butoxycarbonyl-(R)-proline benzyl ester, 87.3 g) as a colorless oil.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.35 (6H, s), 1.46 (3H, s), 1.76-2.04 (3H, m), 2.07-2.31 (1H, m), 3.31-3.61 (2H, m), 4.26 (0.6H, dd, J=8.0 and 3.6Hz), 4.40 (0.4H, dd, J=8.4 and 2.4Hz), 5.04-5.30 (2H, m), 7.25-7.40 (5H, m);
MASS (ES+): m/e 306.13 (M+1).

Preparation 14

To the Compound (13) (114 mg), 4N hydrogen chloride in ethyl acetate (50 ml) was added at ambient temperature and the mixture was stirred at ambient temperature for 2 hours. The mixture was concentrated in vacuo and the residual hydrogen chloride was removed azeotropically with ethyl acetate 4 times.

The residual amorphous solid was dissolved in N,N-dimethylformamide (3 ml), and to the solution were added O-benzyl-N-tert-butoxycarbonyltyrosine (146 mg), 1-ethyl-3-(3'-N,N-dimethylaminopropyl)carbodiimide (63.8 mg) and 1-hydroxybenzotriazole (55.5 mg) under ice-cooling. The mixture was stirred at ambient temperature for 1.5 hours. The mixture was

diluted with ethyl acetate (300 ml) and washed with 5% aqueous potassium hydrogensulfate solution (200 ml, 4 times), saturated aqueous sodium bicarbonate solution (300 ml, twice) and brine (300 ml). The organic layer was dried over anhydrous sodium sulfate, filtered and concentrated in vacuo. The residue was purified by flash chromatography eluted with ethyl acetate-hexane (1:1 v/v) to give Compound (14) (201 mg) as a colorless amorphous solid.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 7.45-7.25 (10H, m), 7.11 (2H, d, J=8Hz), 6.87 (2H, d, J=8Hz), 5.37 (1H, br-d, J=8.4Hz), 5.24-4.95 (2H, m), 4.64-4.52 (1H, m), 4.31 (1H, dd, J=7.3 and 4.8Hz), 3.55-3.45 (2H, m), 3.00 (1H, dd, J=12.8 and 5.6Hz), 2.86 (1H, dd, J=12.8 and 9.6Hz), 2.70-2.55 (1H, m), 1.92-1.70 (2H, m), 1.60 (1H, m), 1.43 (9H, s);

MASS (ES+): m/e 559.36 (M+1).

Preparation 15

To the Compound (14) (6.21 g) was added 4N hydrogen chloride in ethyl acetate (100 ml) under ice-cooling and the mixture was stirred at ambient temperature for one hour. The mixture was concentrated in vacuo and the residual hydrogen chloride was removed 4 times azeotropically with ethyl acetate.

The residual amorphous solid was dissolved in N,N-dimethylformamide (60 ml), then Compound 1 (2.42 g), PyBOP® (6.36 g) (Nova biochem, benzotriazol-1-yloxy-tris-pyrrolidino-phosphonium hexafluorophosphate) and N,N-diisopropylethylamine (4.74 g) were added to this solution, and the resulting mixture was stirred at ambient temperature for 16 hours. The volatiles were removed in vacuo and the residue was extracted with ethyl acetate (500 ml).

The organic phase was washed with aqueous 5% potassium hydrogensulfate solution (100 ml, 4 times), saturated aqueous sodium bicarbonate solution (100 ml, 4 times), water (100 ml) and brine (100 ml). The organic layer was separated, dried over anhydrous sodium sulfate, filtered and concentrated in vacuo. The residue was purified by flash chromatography (eluting with ethyl acetate/hexane = 2:1 v/v) to give Compound (15) (5.10 g) as an amorphous solid.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 7.55-7.20 (10H, m), 7.10 (2H, d, J=7.6Hz), 7.00-6.73 (3H, m), 5.20-4.96 (3H, m), 4.94-4.80 (1H, m),

4.49-4.30 (1H, m), 3.61-3.44 (2H, m), 3.00 (1H, dd, J=13.0 and 5.4Hz), 2.86 (1H, dd, J=13.0 and 8.8Hz), 2.75-2.60 (1H, m), 2.06-1.35 (5H, m), 1.43 (9H, s), 0.80 (3H, t, J=6.3Hz);
MASS (ES+): m/e 658.43 (M+1).

Preparation 16

To the Compound (15) (5.59 g) was added 4N hydrogen chloride in ethyl acetate (50 ml) under ice-cooling and the mixture was stirred at ambient temperature for 1 hour. The mixture was concentrated in vacuo and the residual hydrogen chloride was removed 4 times azeotropically with ethyl acetate.

The residue was dissolved in dichloromethane (50 ml) and to this solution was added Compound b (3.14 g), PyBOP® (4.86 g) and N,N-diisopropylethylamine (3.62 g) under ice-cooling, and the resulting mixture was stirred at ambient temperature for 16 hours. The volatiles were removed in vacuo and the residue was extracted with ethyl acetate (500 ml). The organic phase was washed with 5% aqueous potassium hydrogensulfate solution (200 ml, 4 times), saturated aqueous sodium bicarbonate solution (200 ml, twice), water (200ml, twice) and brine (100 ml). The residue was purified by flash chromatography (eluting with ethyl acetate/hexane = 2:1 v/v) to give Compound (16) (5.2 g) as a colorless amorphous solid.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 8.10-7.98 (2H, m), 7.60-7.22 (13H, m), 7.14-6.77 (5H, m); 6.69 (1H, br-d, J=6.7Hz), 5.18-4.95 (5H, m), 4.93-4.83 (1H, m), 4.39-4.32 (1H, m), 4.31 (2H, t, J=6.6Hz), 4.12-4.02 (1H, m), 3.61-3.49 (2H, m), 3.03-2.85 (2H, m), 2.82-2.70 (1H, m), 2.36-2.19 (1H, m), 1.98-1.38 (10H, m), 1.50 (3H, s), 1.44 (9H, s), 0.72 (3H, t, J=7.3Hz);
MASS (ES+): m/e 891.49 (M).

Preparation 17

A solution of the Compound (16) (5.43 g) in ethyl acetate (110 ml) was hydrogenated in the presence of palladium hydroxide and 20 wt% Pd (dry basis) on carbon (Pearlman's catalyst) (540 mg) for 4 hours under atmosphere pressure. The catalyst was filtered off through a pad of Celite® and the filtrate was concentrated in vacuo. The residue was purified by flash column chromatography eluting with chloroform/methanol = 10:1 v/v to give Compound (17) as a colorless amorphous (4.96 g).
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.78 (3H, t, J=7.0Hz), 1.44 (9H, s), 1.30-2.00 (13H, m), 2.06-2.19 (1H, m), 2.64-2.77 (1H, m), 2.95

(2H, br-d, J=6.6Hz), 3.55-3.69 (1H, m), 3.94-4.07 (1H, m), 4.25-4.38 (3H, m), 4.87 (1H, m), 5.05 (2H, s), 6.82 (1H, s), 6.87 (2H, d, J=8.5Hz), 7.11 (2H, d, J=8.5Hz), 7.20 (1H, br-d, J=8.8Hz), 7.27-7.60 (8H, m), 7.99-8.07 (2H, m);
MASS (ES+): m/e 801.47 (M+1).

Preparation 18

To the Compound (17) (4.96 g) was added 4N hydrogen chloride in ethyl acetate (60 ml) under ice-cooling and the mixture was stirred at ambient temperature for 3 hours. The solvent was concentrated in vacuo and the residual hydrogen chloride was removed azeotropically with ethyl acetate (100 ml, 4 times). The residue was dried in vacuo to give Compound (18) (4.64 g) as a pale brown amorphous solid. The obtained compound was used in the Preparation 75.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.60-0.82 (3H, m), 1.25-2.20 (15H, m), 2.74-3.07 (4H, m), 3.63-3.79 (1H, m), 4.13-4.38 (3H, m), 4.82-4.95 (1H, m), 4.99 (2H, s), 6.83 (2H, d, J=7.3Hz), 7.10 (2H, d, J=7.3Hz), 7.20-7.54 (8H, m), 7.51 (1H, t, J=8.1Hz), 7.57-7.70 (1H, m), 7.99 (2H, d, J=7.0Hz), 8.07-8.40 (2H, m);
MASS (ES+): m/e 701.36 (free+1).

Preparation 19

The Compound (13) (10.0 g) was dissolved in ethyl acetate (60 ml) and the mixture was stirred for 4 hours at ambient temperature. The solvent was evaporated and the residual solvent was removed azeotropically with toluene. The residue was washed with ethyl acetate and dried to give D-proline benzyl ester hydrochloride (hereinafter Compound 19).

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.92 (2H, m), 2.01 (1H, m), 2.28 (1H, m), 3.22 (1H, m), 4.44 (1H, dd, J=8 and 7Hz), 5.23 (1H, d, J=12Hz), 5.26 (1H, d, J=12Hz), 7.23-7.47 (5H, m);
MASS (ES+): m/e 206.

Preparation 20

N-t-Butoxycarbonyl O-methyl-L-tyrosine (3.62 g) was dissolved in dichloromethane (40 ml), then Compound 19 (2.82 g), hydroxybenzotriazol (1.73 g) and a solution of 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide hydrogen chloride (1.99 g) in dichloromethane (5 ml) were added to the mixture and the mixture was stirred for 14 hours at ambient temperature. The reaction mixture was added to 10% aqueous solution of citric acid (50 ml)

then 5% aqueous solution of potassium hydrogensulfate (50 ml) was added to the mixture. The mixture was washed with saturated aqueous sodium bicarbonate (50 ml) and saturated aqueous sodium chloride (50 ml) then dried over magnesium sulfate, and evaporated to dryness to give a crude compound. The crude compound was purified by flash column chromatography (Silica gel 60, Spherical, 120 g, eluent: ethyl acetate : hexane = 1:2 to 1:1) to give Compound (20) (5.55 g).

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.43 (3x3H, s), 1.55 (1H, m), 1.74-2.00 (3H, m), 2.69 (1H, m), 2.87 (1H, dd, J=13.9Hz), 3.00 (1H, dd, J=13 and 5Hz), 3.54 (1H, m), 4.36 (1H ,dd, J=8 and 4Hz), 4.60 (1H, m), 5.11 (1H, d, J=12.5Hz), 5.19 (1H, d, J=12.5Hz), 5.37 (1H, d, J=9Hz), 6.79 (2X1H, d, J=8.5Hz), 7.12 (2X1H, d, J=8.5Hz), 7.28-7.40 (5H, m);

MASS (ES+): m/e 483.

Preparation 21

The Compound (20) (5.50 g) was dissolved in ethyl acetate (30 ml) and a cold solution of 4N hydrogen chloride in ethyl acetate (50 ml) was added to the mixture and stirred for 2.5 hours at ambient temperature. The mixture was evaporated to dryness to give Compound (21) (4.97 g) as a white foam.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.60 (1H, m), 1.70-1.87 (2H, m), 1.97 (1H, m), 2.80 (1H, m), 2.91 (1H, dd, J=13 and 8Hz), 3.06 (1H, dd, J=13 and 6Hz), 3.58 (1H, m), 4.30 (1H, dd, J=9 and 3Hz), 4.36 (1H, m), 5.08 (1H, d, J=13Hz), 5.19 (1H, d, J=13Hz), 6.90 (2 X 1H, d, J=8Hz), 7.14 (2 X 1H, d, J=8Hz), 7.30-7.44 (5H, m), 8.34 (2H, br);

MS (ES+): m/e 383.

Preparation 22

The Compound (21) (4.89 g) was dissolved in dichloromethane (40 ml) and Compound a (4.31g), benzotriazol-1-yloxy-tris-pyrrolidinophosphonium hexafluorophosphate (6.68 g) and N-ethyldiisopropylamine (4.83 g) were added to the solution, and the mixture was stirred for 15 hours at ambient temperature. The mixture was diluted with chloroform (40 ml), washed with 5% aqueous solution of potassium hydrogensulfate (50 ml), saturated sodium bicarbonate (50 ml) and saturated sodium chloride (50 ml), dried over sodium sulfate and evaporated to give a crude compound. The crude compound was purified by flash column chromatography

(Silica gel 60N, Spherical, 120 g, eluent: ethyl acetate : hexane = 1:2 to 1:1) to give Compound (22) (5.70 g).
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.81 (3H, t, J=7.5Hz), 1,41 (3H, s), 1,44 (9H, s), 1.58 (1H, m), 1.76-2.06 (5H, m), 2.75 (1H, m), 2.89 (1H, dd, J=13 and 9Hz), 3.02 (1H, dd, J=13 and 5Hz), 3.56 (1H, m), 3.77 (3H, s), 4.38 (1H, dd, J=8 and 4Hz), 4.91 (1H, ddd, J=9, 8.5 and 5Hz), 5.11 (1H, d, J=12.5Hz), 5.15 (1H, d, J=12.5Hz), 6.80 (2H, d, J=8.5Hz), 6.84 (1H, d, J=8.5Hz), 7.13 (2H, d, J=8.5Hz), 7.28-7.40 (5H, m);
MASS (ES+): m/e 582.

Preparation 23

The Compound (22) (5.31 g) was dissolved in ethyl acetate (30 ml) and cold solution of 4N hydrogen chloride in ethyl acetate (50 ml) was added to the mixture and stirred for 1 hour at ambient temperature. The mixture was evaporated to dryness to give Compound (23) (5.31 g) as a white foam.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.75 (3H, d, J=7Hz), 1.33 (3H, s), 1.63-2.30 (6H, m), 2.84 (1H, dd, J=13 and 10Hz), 2.93 (1H, dd, J=13 and 5Hz), 3.51 (1H, m), 3.74 (1H, m), 4.34 (1H, dd, J=9 and 4Hz), 4.80 (1H, ddd, J=9Hz), 7.20 (2 X 1H, d, J=9Hz), 7.29-7.45 (1H, m), 8.03 (2H, br-s), 8.64 (1H, d, J=9Hz);
MS (ES+): m/e 482.

Preparation 24

The Compound (23) (5.26 g) was dissolved in dichloromethane (30 ml) and a solution of Compound (5) (3.57g) in dichloromethane (50 ml), benzotriazol-1-yloxy-tris-pyrrolidinophosphonium hexafluorophosphate (6.34 g) and N-ethyldiisopropylamine (4.2 g) were added to the solution, and the mixture was stirred for 12 hours at ambient temperature. The mixture was diluted with chloroform (80 ml), washed with 5% aqueous solution of potassium hydrogensulfate (100 ml), saturated sodium bicarbonate (100 ml) and saturated sodium chloride (100 ml), dried over sodium sulfate and evaporated to give a crude compound. The crude compound was purified by flash column chromatography (Silica gel 60N, Spherical, 150 g, eluent: ethyl acetate : hexane = 1:1 to 1:2) to give Compound (24) (5.76 g).
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.72 (3H, t, J=7.3Hz), 1.43 (3H, s), 1.44 (3X3H, s), 1.47-2.36 (12H, m), 2.84 (1H, m), 2.92 (1H, dd, J=13 and 9.5Hz), 2.98 (1H, dd, J=13 and 5.5Hz), 3.58 (1H, m),

3.77 (3H, s), 4.08 (1H, m), 4.32 (2H, t, J=6.5Hz), 4.39 (1H, dd, J=8 and 4Hz), 4.91 (1H, m), 5.12 (1H, m), 5.13 (2H, s), 6.70 (1H, br-d, J=9Hz), 6.80 (2X1H, d, J=8.5Hz), 7.01 (1H, s), 7.10 (2X1H, d, J=8.5Hz), 7.28-7.36 (5H, m), 7.43 (2X1H, dd, J=7.5 and 7.5Hz), 7.55 (1H, dd, J=7.5 and 7.5Hz), 8.03 (2X1H, d, J=7.5Hz);
MASS (ES-): m/e 813.

Preparation 25

Compound (25) was obtained in a manner similar to Preparation 17 except that Compound (24) was used instead of the Compound (16) and palladium on carbon was used instead of the Pearlman's catalyst.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.77 (3H, t, J=7.5Hz), 1.38-2.36 (12H, m), 1.44 (9+3H, s), 2.79 (1H, m), 2.90-3.02 (2H, m), 3.67 (1H, m), 3.77 (3H, s), 4.02 (1H, m), 4.26-4.42 (3H, m), 4.88 (1H, m), 5.20 (1H, m), 6.81 (2X1H, d, J=8.5Hz), 6.83 (1H, br-s), 7.12 (2X1H, d, J=8.5Hz), 7.24 (1H, d, J=8Hz), 7.43 (2X1H, dd, J=7.5 and 7.5Hz), 7.56 (1H, dd, J=7.5 and 7.5Hz), 8.04 (2X1H, d, J=7.5Hz);
MASS (ES-): m/e 723.

Preparation 26

Compound (26) was obtained in a manner similar to Preparation 18 except that trifluoroacetic acid was used instead of 4N hydrogen chloride. The obtained compound was used in Preparation 78.

^{1}H-NMR (300MHz, DMSO-d_6, δ): 0.54 (3X1/3H, t, J=7.3Hz, 0.66 (3X2/3H, t, J=7.3Hz), 1.31 (3X1/3H, s), 1.35 (3X2/3H, s), 1.44 (2H, m), 1.60-2.20 (10H, m), 2.70-2.98 (2H, m), 3.18 (1H, m), 3.36 (1H, m), 3.67 (3X1/3H, s), 3.69 (3X2/3H, s), 4.12 (1X2/3H, dd, J=9.3Hz), 4.26 (2H, t, J=6Hz), 4.41 (1H, m), 4.77 (1H, m), 4.84 (1X1/3H, dd, J=9.3Hz), 6.78 (2X1/3H, d, J=9Hz), 6.81 (2X2/3H, d, J=9Hz), 7.10-7.30 (3H, m), 7.48-7.60 (2H, m), 7.68 (1H, m), 7.88-8.17 (5H, m);
MASS (ES+): m/e 625.

Preparation 27

Compound (27) was obtained in a manner similar to Preparation (14).

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.42 (9H, s), 1.50-1.68 (1H, m), 1.80-2.03 (3H, m), 2.71-2.84 (1H, m), 2.92 (1H, dd, J=13.2 and 8.7Hz), 3.00 (1H, dd, J=13.2 and 6.1Hz), 3.53-3.65 (1H, m), 4.36 (1H, dd, J=7.7 and 3.6Hz), 4.62 (1H, dt, J=8.5 and 5.9Hz), 5.10 (1H, d,

J=12.5Hz), 5.20 (1H, d, J=12.5Hz), 5.34 (1H, d, J=8.0Hz), 6.88-7.03 (2H, m), 7.17 (2H, dd, J=8.5 and 5.5Hz), 7.30-7.40 (5H, m); MASS (ES+): m/e 471.37 (M+1).

Preparation 28

Compound (28) was obtained in a manner similar to Preparation 15.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.80 (3H, t, J=7.6Hz), 1.39 (3H, s), 1.43 (9H, s), 1.76-2.03 (6H, m), 2.74-2.87 (1H, m), 2.95 (1H, dd, J=13.2 and 9.1Hz), 3.03 (1H, dd, J=13.2 and 4.8Hz), 3.51-3.66 (1H, m), 4.38 (1H, dd, J=8.1 and 3.7Hz), 4.87-4.98 (1H, m), 4.98-5.20 (3H, m), 6.81-7.02 (3H, m), 7.15-7.23 (2H, m), 7.28-7.41 (5H, m); MASS (ES+): m/e 570.42 (M+1).

Preparation 29

Compound (29) was obtained in a manner similar to Preparation 15.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.61 (0.6H, t, J=7.3Hz), 0.72 (2.4H, t, J=7.3Hz), 1.39-2.08 (11H, m), 1.43 (9H, s), 1.48 (3H, s), 2.13-2.33 (1H, m), 2.83-2.99 (1H, m), 2.98 (2H, d, J=7.0Hz), 3.51-3.70 (1H, m), 3.92-4.15 (1H, m), 4.31 (2H, t, J=5.9Hz), 4.39 (1H, dd, J=7.3 and 3.2Hz), 4.92 (1H, q, J=7.3Hz), 5.02-5.15 (2H, m), 5.17 (1H, s), 6.72 (1H, br. s), 6.83-7.05 (3H, m), 7.16 (2H, dd, J=8.4 and 5.5Hz), 7.27-7.38 (5H, m), 7.39-7.47 (2H, m), 7.51-7.60 (1H, m), 8.03 (2H, d, J=7.3Hz);

MASS (ES+): m/e 803.55 (M+1).

Preparation 30

Compound (30) was obtained in a manner similar to Preparation 17.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.77 (3H, t, J=7.4Hz), 1.17-2.02 (11H, m), 1.45 (12H, s), 2.11-2.25 (1H, m), 2.79-3.10 (3H, m), 3.64-3.79 (1H, m), 4.26-4.42 (3H, m), 4.92 (1H, q, J=7.6Hz), 5.23 (1H, br.s), 6.79 (1H, br.s), 6.97 (2H, t, J=8.5Hz), 7.19 (2H ,dd, J=8.5 and 5.2Hz), 7.30 (1H, d, J=8.3Hz), 7.39-7.48 (2H, m), 7.52-7.62 (1H, m), 8.04 (2H, d, J=8.5Hz);

MASS (ES+): m/e 713.54 (M+1).

Preparation 31

Compound (31) was obtained in a manner similar to Preparation 18. The obtained compound was used in Preparation 81.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.70 (3H, t, J=7.4Hz), 1.38 (3H, s), 1.51-2.16 (12H, m), 2.83-3.15 (3H, m), 3.68-3.83 (1H, m), 4.18-

4.37 (4H, m), 4.86-4.98 (1H, m), 6.92 (2H, t, J=8.5Hz), 7.17 (2H, dd, J=8.5 and 5.8Hz), 7.39 (2H, t, J=7.7Hz), 7.53 (1H, t, J=7.6Hz), 7.67 (1H, br. s), 7.99 (2H, d, J=7.3Hz), 8.13-8.39 (3H, m);

MASS (ES+): m/e 613.49 (M+1, free).

Preparation 32

Compound (32) was obtained in a manner similar to Preparation 14.

Preparation 33

Compound (33) was obtained in a manner similar to Preparation 15.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.31-1.54 (9H, m), 1.55-1.99 (8H, m), 2.01-2.42 (3H, m), 2.52-2.63 (1H, m), 2.80-2.96 (1H, m), 3.03-3.14 (1H, m), 3.44-3.60 (2H, m), 4.31-4,38 (1H, m), 4.68-4.86 (1H, m), 4.94 (1H, dt, J=9.9 and 5.1Hz), 5.05-5.20 (2H, m), 7.08 (1H, d, J=8.1Hz), 7.16-7.39 (10H, m);

MASS (ES+): m/e 564.38 (M+1).

Preparation 34

Compound (34) was obtained in a manner similar to Preparation 16.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.32-2.06 (20H, m), 1.44 (9H, s), 2.09-2.30 (2H, m), 2.64-2.74 (1H, m), 2.88-3.08 (1H, m), 3.53-3.62 (2H, m), 3.98-4.08 (1H, m), 4.27-4.37 (4H, m), 4.85-4.95 (1H, m), 5.07-5.21 (3H, m), 6.63 (1H, s), 7.12-7.37 (6H, m), 7.42 (2H, dd, J=8.1 and 6.9Hz), 7.55 (1H, dd, J=6.9 and 6.9Hz), 8.03 (2H, d, J=8.1Hz);

MASS (ES+): m/e 797.50 (M+1).

Preparation 35

Compound (35) was obtained in a manner similar to Preparation 17.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.16-2.12 (15H, m), 1.44 (9H, s), 2.24-2.41 (1H, m), 2.62-2.76 (1H, m), 2.90-3.09 (2H, m), 3.47-3.50 (1H, m), 3.65-3.77 (1H, m), 4.01-4.11 (2H, m), 4.24-4.38 (4H, m), 4.74-4.84 (1H, m), 5.56-5.64 (1H, m), 6.84-6.92 (1H, m), 7.16-7.31 (6H, m), 7.43 (2H, dd, J=7.8 and 6.9Hz), 7.56 (1H, dd, J=7.8 and 7.8Hz), 8.02 (2H, d, J=6.9Hz);

MASS (ES+): m/e 707.45 (M+1).

Preparation 36

Compound (36) was obtained in a manner similar to

Preparation 18. The obtained compound was used in Preparation 84. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.34-2.27 (19H, m), 2.79-3.19 (3H, m), 3.48-3.78 (1H, m), 3.95-4.13 (1H, m), 4.14-4.47 (3H, m), 4.82-5.00 (1H, m), 7.11-7.32 (5H, m), 7.34-7.46 (2H, m), 7.48-7.58 (1H, m), 7.62-7.84 (1H, br. s), 7.95-8.06 (2H, m), 8.06-8.36 (2H, br. s), 8.63-9.02 (1H, br. s);
MASS (ES+): m/e 607.42 (M+1).

<u>Preparation 37</u>

Compound (37) was obtained in a manner similar to Preparation 19.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.31 (3H, s), 1.40 (6H, s), 1.56-1.80 (3H, m), 1.84-2.11 (2H, m), 2.92-3.13 (2H, m), 3.57-3.70 (1H, m), 4.36-4.42 (1H, m), 4.62-4.72 (1H, m), 5.04-5.34 (3H, m), 7.11-7.51 (7H, m), 7.54-7.60 (3H, m);
MASS (ES+): m/e 478.40 (M+1).

<u>Preparation 38</u>

Compound (38) was obtained in a manner similar to Preparation 15.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.800 (3H, t, J=7.5Hz), 1.36 (3H, s), 1.39 (3H, s), 1.43 (6H, s), 1.52-1.62 (2H, m), 1.67-2.06 (4H, m), 2.83-3.16 (2H, m), 3.50-3.70 (2H, m), 4.36-4.42 (1H, m), 4.86-5.04 (2H, m), 5.06-5.21 (2H, m), 6.87 (1H, d, J=9.0Hz), 7.29-7.48 (6H, m), 7.53-7.59 (3H, m);
MASS (ES+): m/e 577.40 (M+1).

<u>Preparation 39</u>

Compound (39) was obtained in a manner similar to Preparation 16.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.740 (3H, t, J=7.2Hz), 1.30-2.29 (11H, m), 1.34 (3H, s), 1.44 (9H, s), 2.86-3.18 (3H, m), 3.51-3.72 (2H, m), 3.99-4.08 (1H, m), 4.27-4.42 (3H, m), 4.96-5.04 (1H, m), 5.06-5.19 (3H, m), 6.82 (1H, s), 7.12-7.17 (1H, m), 7.28-7.37 (6H, m), 7.39-7.47 (3H, m), 7.52-7.61 (3H, m), 8.00-8.05 (2H, m);
MASS (ES+): m/e 810.59 (M+1).

<u>Preparation 40</u>

Compound (40) was obtained in a manner similar to Preparation 17.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.731 (3H, t, J=7.2Hz), 1.31-2.22 (13H, m), 1.40 (3H, s), 1.44 (9H, s), 2.91-3.23 (3H, m), 3.80-3.94 (1H, m), 3.99-4.13 (1H, m), 4.23-4.43 (3H, m), 4.86-5.00 (1H, m),

5.48-5.60 (1H, m), 6.76 (1H, s), 7.25-7.31 (1H, m), 7.31-7.38 (2H, m), 7.40-7.47 (2H, m), 7.52-7.61 (3H, m), 8.00-8.06 (2H, m);
MASS (ES+): m/e 720.38 (M+1).

Preparation 41

Compound (41) was obtained in a manner similar to Preparation 18. The obtained compound was used in Preparation C5.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.59-0.73 (3H, m), 1.33 (3H, s), 1.52-2.17 (12H, m), 2.92-3.27 (3H, m), 3.70-3.83 (1H, m), 4.14-4.40 (4H, m), 4.90-5.02 (1H, m), 7.31-7.45 (5H, m), 7.49-7.59 (3H, m), 7.59-7.71 (1H, br. s), 7.93-8.11 (5H, m);
MASS (ES+): m/e 620.33 (M+1).

Preparation 42

Compound (42) was obtained in a manner similar to Preparation 19.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.39 (3H, t, J=7.2Hz), 1.43 (9H, s), 1.46-1.63 (1H, m), 1.76-2.00 (3H, m), 2.62-2.72 (1H, m), 2.82-2.92 (1H, m), 2.94-3.04 (1H, m), 3.48-3.58 (1H, m), 3.98 (2H, q, J=7.2Hz), 4.32-4.42 (1H, m), 4.53-4.64 (1H, m), 5.10 (1H, d, J=12.6Hz), 5.20 (1H, d, J=12.6Hz), 5.37 (1H, d, J=8.7Hz), 6.78 (2H, d, J=8.7Hz), 7.11 (2H, d, J=8.7Hz), 7.28-7.39 (5H, m);
MASS (ES+): m/e 497.34 (M+1).

Preparation 43

Compound (43) was obtained in a manner similar to Preparation 15.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.80 (3H, t, J=7.5Hz), 1.39 (3H, t, J=7.2Hz), 1.40 (3H, s), 1.43 (9H, s), 1.50-1.64 (1H, m), 1.75-2.05 (5H, m), 2.67-2.79 (1H, m), 2.81-2.93 (1H, m), 2.94-3.05 (1H, m), 3.50-3.62 (1H, m), 3.98 (2H, q, J=7.2Hz), 4.37 (1H, dd, J=7.5 and 3.3Hz), 4.90 (1H, dt, J=9.6 and 5.1Hz), 5.10 (1H, d, J=12.3Hz), 5.15 (1H, d, J=12.3Hz), 6.57-6.97 (1H, m), 6.78 (2H, d, J=8.4Hz), 7.11 (2H, d, J=8.4Hz), 7.29-7.39 (5H, m);
MASS (ES+): m/e 596.51 (M+1).

Preparation 44

Compound (44) was obtained in a manner similar to Preparation 16.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.74 (3H, t, J=7.5Hz), 1.40 (3H, t, J=7.2Hz), 1.45 (9H, s), 1.47-1.99 (11H, m), 1.50 (3H, s), 2.18-2.29 (1H, m), 2.76-3.00 (2H, m), 3.44-3.65 (2H, m), 3.99 (2H, q, J=7.2Hz), 4.03-4.13 (1H, m), 4.33 (2H, t, J=6.3Hz), 4.40 (1H, dd,

J=7.2 and 3.6Hz), 4.83-4.94 (1H, m), 5.10-5.19 (3H, m), 6.79 (2H, d, J=8.4Hz), 6.92-7.04 (1H, m), 7.10 (2H, d, J=8.4Hz), 7.29-7.39 (6H, m), 7.40-7.48 (2H, m), 7.52-7.60 (1H, m), 8.01-8.07 (2H, m); MASS (ES+): m/e 829.61 (M+1).

Preparation 45

Compound (45) was obtained in a manner similar to Preparation 17.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.79 (3H, t, J=7.5Hz), 1.40 (3H, t, J=7.2Hz), 1.44 (12H, s), 1.57-2.72 (11H, m), 2.65-3.03 (3H, m), 3.58-3.83 (2H, m), 3.99 (2H, q, J=7.2Hz), 4.04-4.15 (1H, m), 4.23-4.39 (3H, m), 4.75-4.88 (1H, m), 5.53-5.63 (1H, m), 6.79 (2H, d, J=8.7Hz), 7.09 (2H, d, J=8.7Hz), 7.13-7.21 (1H, m), 7.39-7.48 (2H, m), 7.52-7.59 (1H, m), 8.00-8.06 (2H, m);
MASS (ES+): m/e 739.58 (M+1).

Preparation 46

Compound (46) was obtained in a manner similar to Preparation 18. The obtained compound was used in Preparation 91.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.72 (3H, t, J=6.9Hz), 1.34 (3H, s), 1.38 (3H, t, J=7.2Hz), 1.54-2.13 (12H, m), 2.80-3.18 (3H, m), 3.64-3.78 (1H, m), 3.36 (2H, q, J=7.2Hz), 4.14-4.38 (4H, m), 4.77-4.89 (1H, m), 6.77 (2H, d, J=8.7Hz), 7.09 (2H, d, J=8.7Hz), 7.37-7.48 (2H, m), 7.49-7.57 (1H, m), 7.80-8.22 (6H, m);
MASS (ES+): m/e 739.58 (free M+1).

Preparation 47

Compound (47) was purchased from Kokusan Chemical Co., Ltd.

Preparation 48

Fmoc-2-fluorophenylalanine (available from Oakwood Products, Inc.), 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide hydrochloride (1.29 g) and 1-hydroxybenzotriazole (911 mg) were added to dichloroethane (30 ml), and the mixture was sonicated to give a homogeneous mixture. To this mixture, Compound (47) (1.05 g) in dichloromethane (10 ml) was added and stirred at ambient temperature for 1.3 hours. The reaction mixture was added to 10% aqueous citric acid (30 ml), then the organic layer was collected. To the aqueous layer water (30 ml) was added, then the mixture was extracted with chloroform (50 ml). The organic layer and the chloroform extract were combined, washed with saturated sodium bicarbonate (30 ml) and brine (30 ml), dried over magnesium sulfate, and the solvent was evaporated to give a crude compound.

The crude compound was purified by flash column chromatography (Silica gel 60, Spherical, 40g, eluted with ethyl acetate/hexane = 1:2 to 1:1 v/v) to give Compound (48) (3.29 g) as a white foam.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.43 (9x4/5H, s), 1.51 (9x1/5H, s), 1.63-2.30 (4H, m), 3.00-3.14 (2H, m), 3.20 (1H, m), 3.70 (1H, m), 4.04-4.42 (4H, m), 4.58 (1x1/5H, m), 4.82 (1x4/5H, m), 5.48 (1x4/5H, d, J=8Hz), 5.71 (1x1/5H, d, J=8Hz), 6.95-7.08 (2H, m), 7.11-7.62 (8H, m), 7.71-7.80 (2H, m);
MASS (ES+): m/e 559.

Preparation 49

The Compound (48) (3.25 g) was dissolved in acetonitrile (15 ml), N,N-diethylamine (15 ml) was added to the mixture and stirred for 1 hour at ambient temperature. The solvent was evaporated and the residual solvent was removed azeotropically with toluene to give a crude compound. The crude compound was purified by flash column chromatography (Silica gel 60, Spherical, 40-50 μm, eluted with methanol/chloroform = 1:40 v/v) to give Compound (49) (1.52 g) as a white foam.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.46 (9 X 5/6H, s), 1.47 (9 X 1/6H, s), 1.56-2.25 (4H, m), 2.79 (1 X 1/6H, dd, J=13 and 8Hz), 2.83 (1 X 5/6H, dd, J=13 and 8Hz), 2.94 (1 X 5/6H, dd, J=13 and 7Hz), 3.10 (1 X 1/6H, dd, J=13 and 5Hz), 3.19 (1H, m), 3.62 (1H, m), 3.83 (1H, d, J=8 and 7Hz), 4.28 (1 X 5/6H, dd, J=8 and 4Hz), 4.60 (1 X 1/6H, dd, J=8 and 3Hz), 6.98-7.12 (2H, m), 7.17-7.28 (2H, m);
MASS (ES+): m/e 337.

Preparation 50

The Compound (49) (1.51 g) was dissolved in dichloromethane (20 ml) and 2(S)-ethyl-2-benzyloxycarbonylaminopropionic acid (1.13g), PyBroP® (2.3 g) and N-ethyl-N,N-diisopropylamine (696 mg) were added to the solution, and the mixture was stirred for 5 hours at ambient temperature. The mixture was washed with 10% aqueous solution of citric acid (30 ml), saturated sodium bicarbonate (30 ml) and saturated sodium chloride (30 ml), dried over magnesium sulfate and the solvent was evaporated to give a crude compound. The crude compound was purified by flash column chromatography (Silica gel 60N, Spherical, 40 g, eluent: ethyl acetate : hexane = 1:2 to 1:1) to give Compound (50) (1.54 g).
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.60 (3x1/4H, t, J=7Hz), 0.75 (3x3/4H, t, J=7.3Hz), 1.33-2.30 (18H, m), 2.98-3.32 (3H, m), 3.50-3.80 (1H,

m), 4.25 (1x3/4H, dd, J=8 and 4Hz), 4.67-5.10 (3+1/4H, m), 5.53 (1x1/4H, br), 5.78 (1x3/4H, br), 6.57 (1x1/4H, br), 6.73 (1x3/4H, br-d, J=8Hz), 6.94-7.07 (2H, m), 7.11-7.24 (2H, m), 7.28-7.39 (5H, m);

MASS (ES+): m/e 570.

Preparation 51

The Compound (50) (1.52 g) was dissolved in methanol and 10% palladium on carbon (150 mg) suspended in water (1 ml) was added to the solution and stirred for 2 hours at ambient temperature, 3 atm. The catalyst was filtered off through a pad of Celite®, the solvent was evaporated, then the residual solvent was removed azeotropically with toluene to give Compound (51).

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.42 (3 X 1/3H, t, J=7.4Hz), 0.72 (3 X 2/3H, t, J=7.5Hz), 1.19 (3 X 1/3H, s), 1.26 (3 X 2/3H, s), 1.43 (9 X 2/3H, s), 1.51 (9 X 1/3H, s), 1.69-2.30 (6H, m), 2.99-3.30 (3H, m), 3.56-3.77 (1H, m), 4.25 (1 X 2/3H, dd, J=8 and 4Hz), 4.71 (1 X 1/3H, m), 5.02 (1 X 2/3H, m), 5.04 (1 X 1/3H, m), 6.93-7.08 (2H, m), 7.12-7.25 (2H, m);

MASS (ES+): m/e 436.

Preparation 52

The Compound (51) (1.15 g) was dissolved in dichloromethane (15 ml) and a solution of Compound (5) (1.02 g) in dichloromethane (10 ml), benzotriazole-1-yloxy-tris-pyrrolidinophosphonium hexafluorophosphate (1.65 g) and N-ethyl-N,N-diisopropylamine (751 mg) were added to the solution, and the mixture was stirred for 14 hours at ambient temperature. The mixture was washed with 10% aqueous solution of citric acid (30 ml), saturated sodium bicarbonate (30 ml) and saturated sodium chloride (30 ml), dried over sodium sulfate and the solvent was evaporated to give a crude compound. The crude compound was purified by flash column chromatography (Silica gel 60, Spherical, 50 g, eluent: ethyl acetate : hexane = 1:1 to 2:1) to give Compound (52) (1.74 g) as a white foam.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.60 (3x1/3H, t, J=7.5Hz), 0.71 (3x2/3H, t, J=7.5Hz), 1.34-2.44 (12H, m), 1.41 (9x2/3H, s), 1.43 (9x1/3H, s), 1.49 (3x1/3H, s), 1.51 (3x2/3H, s), 3.00-3.12 (2H, m), 3.23-3.76 (2H, m), 4.07 (1H, m), 4.25 (1H, dd, J=8 and 4Hz), 4.31 (2H, t, J=6.5Hz), 4.67-5.17 (2H, m), 6.54 (1x1/3H, br-d, J=8Hz), 6.70 (1x2/3H, br-d, J=8Hz), 6.93-7.09 (3H, m), 7.10-7.25

(2H, m), 7.43 (2H, dd, J=7.5 and 7.5Hz), 7.56 (1H, dd, J=7.5 and 7.5Hz), 8.03 (2H, d, J=7.5Hz);
MASS (ES-): m/e 767.

Preparation 53

Compound (53) was obtained in a manner similar to Preparation 18 except that trifluoroacetic acid was used instead of 4N hydrogen chloride. The obtained compound was used in Preparation 93.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.62 (3H, t, J=7.3Hz), 1.20 (3H, s), 1.49-2.15 (12H, m), 2.88-3.10 (2H, m), 3.34 (1H, m), 3.82 (1H, m), 4.07 (1H, m), 4.23-4.38 (3H, m), 4.92 (1H, m), 6.96-7.11 (2H, m), 7.14-7.28 (3H, m), 7.42 (2H, dd, J=7.6 and 7.6Hz), 7.50-7.58 (2H, m), 7.82 (2H, br), 8.01 (2H, d, J=7.6Hz);
MASS (ES+): m/e 613.

Preparation 54

Compound (54) was obtained in a manner similar to Preparation 18. The obtained compound was used in Preparation 96.

Preparation 55

Compound (55) was obtained in a manner similar to Preparation 18. The obtained compound was used in Preparation 99.

Preparation 56

Compound (56) was obtained in a manner similar to Preparation 16.

Preparation 57

Compound (57) was obtained in a manner similar to Preparation 18 except that trifluoroacetic acid was used instead of 4N hydrogen chloride. The obtained compound was used in Preparation 102.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.70 (3H, t, J=7Hz), 1.27 (3H, s), 1.49-2.10 (12H, m), 2.85-3.05 (3H, m), 3.70 (1H, m), 4.09 (1H, m), 4.24 (1H, m), 4.27-4.40 (2H, m), 4.83 (1H, m), 7.13-7.34 (5H, m), 7.42 (2X1H, dd, J=8.8Hz), 7.55 (1H, m), 7.80 (2H, br), 7.89 (1H, s), 8.00 (2X1H, dd, J=8 and 1Hz);
MASS (ES+): m/e 595.

Preparation 58

Compound (58) was obtained in a manner similar to Preparation 18. The obtained compound was used in Preparation 105.

Preparation 59

Compound (59) was obtained in a manner similar to

Preparation 14.

Preparation 60

The Compound (59) (600 mg) was dissolved in dichloromethane (10 ml), tert-butoxycarbonyl-D-tert-leucine (444 mg), a solution of 1-ethyl-3-(3'-N,N-dimethylaminopropyl)carbodiimide (328 mg) in dichloromethane (2 ml) and hydroxybenzotriazole (285 mg) were added to the solution, and stirred for 15 hours at ambient temperature. The mixture was washed with 10% aqueous solution of citric acid (10 ml), water (20 ml), saturated sodium bicarbonate (20 ml) and saturated sodium chloride (20 ml), dried over sodium sulfate and the solvent was evaporated to give a crude compound as pale yellow oil. The crude compound was purified by flash column chromatography (Kieselgel 60, 30 g, eluent: ethyl acetate : hexane = 1:2 to 1:1) to give Compound (60) (669 mg) as a white foam.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.60 (9x1/3H, s), 0.74 (9x2/3H, s), 1.36 (9x1/3H, s), 1.38 (9x2/3H, s), 1.64-2.30 (4H, m), 2.75-2.89 (1+1/3H, m), 2.93 (1x2/3H, dd, J=13.5 and 6.5Hz), 3.16-3.72 (2H, m), 3.84 (1x1/3H, d, J=10Hz), 3.90 (1x2/3H, d, J=10Hz), 4.17 (1x2/3H, dd, J=8,4Hz), 4.38 (1x1/3H, m), 4.80 (1x2/3H, m), 5.10 (1x1/3H, m), 6.40 (1x1/3H, d, J=10Hz), 6.47 (1x2/3H, d, J=10Hz), 7.12-7.30 (5H, m), 8.31 (1x2/3H, d, J=8Hz), 8.65 (1x1/3H, d, J=8Hz);

MASS (ES+): m/e 490.

Preparation 61

The Compound (61) (297 mg) was dissolved in dioxane (3 ml) and cold solution of 4N hydrogen chloride in dioxane (3 ml) was added to the mixture and stirred for 12 hours at ambient temperature. The mixture was evaporated to dryness to give Compound (61) (250 mg) as a white powder.

^{1}H-NMR (300MHz, DMSO-d_6 δ): 0.63 (9x1/3H, s), 0.82 (9x2/3H, s), 1.60-2.30 (4H, m), 2.79-2.92 (1+1/3H, m), 2.97 (1x2/3H, dd, J=13 and 7Hz), 3.05-3.66 (3H, m), 3.61 (3x2/3H, s), 3.75 (3x1/3H, s), 4.21 (1x2/3H, dd, J=8.5, 3.5Hz), 4.55 (1x1/3H, m), 4.94 (1x2/3H, ddd, J=8, 8, 7Hz), 5.14 (1x1/3H, dd, J=8, 4Hz), 7.12-7.33 (5H, m), 8.10 (2H, br), 8.80 (1x2/3H, d, J=8Hz), 9.03 (1x1/3H, d, J=8Hz);

MASS (ES+): m/e 390.

Preparation 62

The Compound (61) (227 mg) was dissolved in dichloromethane

(3 ml) and a solution of Compound (12) (217 mg) in dichloromethane (2 ml), hydroxybenzotriazole (86.4 mg) and a solution of 1-ethyl-3-(3'-N,N-dimethylaminopropyl)carbodiimide (99.3 mg) in dichloromethane (3 ml) were added to the solution, and the mixture was stirred for 15 hours at ambient temperature. The mixture was washed with 10% aqueous solution of citric acid (20 ml), saturated sodium bicarbonate (20 ml) and saturated sodium chloride (20 ml), dried over sodium sulfate and the solvent was evaporated to give a crude compound. The crude compound was purified by preparative thin layer chromatography (Merck Art 5717 x 2 plates, eluent: ethyl acetate : hexane = 1:1) to give Compound (62) (297 mg) as a white foam.

^{1}H-NMR (300MHz, DMSO-d_6 δ): 0.55 (9X1/3H, s), 0.70 (9X2/3H, s), 1.10-1.90 (10H, m), 1.22 (3H, d, J=7Hz), 1.36 (9H, s), 1.93-2.33 (2H, m), 2.40-2.60 (2H, m), 2.71-2.89 (1+1/3H, m), 2.94 (1X2/3H, dd, J=13.7Hz), 3.18-3.73 (2H, m), 3.53 (3X2/3H, s), 3.74 (3X1/3H, s), 3.95 (1H, m), 3.97 (1H, q, J=7Hz), 4.16 (1X2/3H, dd, J=8.4Hz), 4.23 (1X1/3H, d, J=10Hz), 4.28 (1X2/3H, d, J=10Hz), 4.45 (1H, d, J=12Hz), 4.49 (1H, d, J=12Hz), 4.82 (1H, m), 5.14 (1X1/3H, m), 6.91 (1X1/3H, m), 6.91 (1X1/3H, d, J-7Hz), 6.95 (1X2/3H, d, J=7Hz), 7.11-7.40 (10H, m), 7.49 (1X1/3H, d, J=10Hz), 7.52 (1X2/3H, d, J=10Hz), 8.50 (1X2/3H, d, J=8Hz), 8.82 (1X1/3H, d, J-8Hz);

MASS (ES-): m/e 777.

<u>Preparation 63</u>

Compound (63) was obtained in a manner similar to Preparation (17) except that 1N sodium hydroxide aqueous solution was used instead of the hydrogenation catalyst.

^{1}H-NMR (300MHz, DMSO-d_6, δ): 0.52 (9X5/9H, s), 0.72 (9X4/9H, s), 1.10-1.90 (10H, m), 1.22 (3H, d, J=7Hz), 1.35 (9X5/9H, s), 1.37 (9X4/9H, s), 2.15 (2H, m), 2.42-2.60 (2H, m), 2.70-3.00 (2H, m), 3.08-3.65 (2H, m), 3.95 (1H, m), 3.96 (1H, q, J=7Hz), 4.10 (1X4/9H, dd, J=8 and 4Hz), 4.24 (1X5/9H, d, J=10Hz), 4.27 (1X4/9H, d, J=10Hz), 4.38 (1X4/9H, m), 4.45 (1H, d, J=12Hz), 4.49 (1H, d, J=12Hz), 4.83 (1X5/9H, m), 5.02 (1X5/9H, m), 6.91 (1X5/9H, d, J=7.5Hz), 6.95 (1X4/9H, d, J=7.5Hz), 7.10-7.40 (10H, m), 7.48 (1X5/9H, brd, J=10Hz), 7.51 (1X4/9H, brd, J=19Hz), 8.41 (1X4/9H, d, J=8Hz), 8.79 (1X5/9H, d, J=8Hz);

MASS (ES-): m/e 763.

Preparation 64

Compound (64) was obtained in a manner similar to Preparation (18). The obtained compound was used in Preparation 108.

^{1}H-NMR (300MHz, DMSO-d_6, δ): 0.52 (9x1/2H, s), 0.73 (9x1/2H, s), 1.10-1.50 (4H, m), 1.21 (3x1/2H, d, J=6.5Hz), 1.22 (3x1/2H, d, J=6.5Hz), 1.58-1.96 (6H, m), 2.12-2.29 (2H, m), 2.35-2.60 (2H, m), 2.70-3.00 (2H, m), 3.06-3.66 (2H, m), 3.95 (1H, m), 3.96 (1x1/2H, q, J=6.5Hz), 3.97 (1x1/2H, q, J=6.5Hz), 4.10 (1x1/2H, m), 4.26-4.54 (3+1/2H, m), 4.85 (1x1/2H, m), 5.06 (1x1/2H, m), 7.14-7.41 (10H, m), 8.09 (2H, br), 8.55 (1x1/2H, d, J=8.5Hz), 8.60 (1x1/2H, d, J=9Hz), 8.67 (1x1/2H, d, J=8Hz), 8.88 (1x1/2H, d, J=7Hz);

MASS (ES-): m/e 663.

Preparation 65

2-Chlorotrityl chloride resin (Nova Biochem, 0.9 mmol Cl/gram, 2.0 g) was washed with dichloromethane (3 ml) for 5 minutes twice. The resin was suspended in dichloromethane (3 ml) and to the suspension were added N-(9-fluorenylmethoxycarbonyl)-(R)-proline (1.82 g) in dichloromethane (3 ml) and N,N-diisopropylethylamine (698 mg). The suspension was shaken using rotary shaker for 15 minutes. Additionally, N,N-diisopropylethylamine (1.05 g) was added to the suspension and the mixture was shaken for 1 hour. The reagents and solvent were washed away and the residual solid was washed with dichloromethane (20 ml, 5 times), N,N-dimethylformamide (20 ml, 3 times), dichloromethane (20 ml, 3 times) and isopropyl alcohol (20 ml). The resulting solid was dried under vacuum to give Compound (65) (2.89 g).

To determine the loading value, the Compound (65) (300 mg) was treated with a mixture of dichloromethane-trifluoroacetic acid (1:1 v/v, 6 ml) for 1 hour. The Compound (65) was filtered and the filtrate was concentrated in vacuo to give 107 mg of N-(9-fluorenylmethoxycarbonyl)-(R)-proline (107 mg) which was identical with the starting material by HPLC analysis. Mightysil RP-18 GP 250-4.6 (5 mm) (Kanto Chemical Co., Ltd.), 0.1% TFA-acetonitrile/0.1% TFA-water 50:50 rt=12.15 minutes.

^{1}H-NMR (300MHz, DMSO-d_6, δ): 1.78-2.34 (4H, m), 3.32-3.50 (2H, m), 4.11-4.37 (4H, m), 7.10-7.38 (3H, m), 7.43 (2H, t, J=7.7Hz), 7.62-7.71 (2H, m), 7.90 (2H, dd, J=7.8 and 4.1Hz).

Preparation 66

A solution of piperidine in N,N-dimethylformamide (20% v/v, 20 ml) was added to the Compound B1-1 (2.00 g) and the resulting suspension was shaken using rotary shaker for 15 minutes. The suspension was filtered and then a solution of piperidine in N,N-dimethylformamide (20% v/v, 20 ml) was added to the residual solid. The suspension was shaken for additional 15 minutes. The suspension was filtered and the residual solid was washed with N,N-dimethylformamide (20 ml, 5 times). To the residual solid were added (S)-N-(9-fluorenylmethoxycarbonyl)phenylalanine (2.46 g), benzotriazole-1-yloxy-tris-pyrrolidinophosphonium hexafluorophosphate (PyBOP®; 3.31 g) and N,N-diisopropylethylamine (822 mg) at ambient temperature and the resulting suspension was shaken at the same temperature for 16 hours. The suspension was filtered and the residual solid was washed with N,N-dimethylformamide (20 ml, 5 times), dichloromethane (20 ml, 3 times) and isopropyl alcohol, and dried to give Compound (66) (2.08 g).

To determine the loading value, the Compound (66) (200 mg) was treated with a mixture of dichloromethane-trifluoroacetic acid (1:1 v/v, 4 ml) for 1 hour. The Compound (66) was filtered and the filtrate was concentrated in vacuo to give a dipeptide compound (79 mg). The purity of the dipeptide compound was determined by HPLC analysis. Mightysil RP-18 GP 250-4.6 (5mm) (Kanto Chemical Co., Ltd.), 0.1% TFA-acetonitrile/0.1% TFA-water 50:50 rt=20.64 minutes.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.50-1.71 (2H, m), 1.74-1.91 (1H, m), 2.16-2,34 (1H, m), 3.00 (1H, dd, J=12.5 and 9.6Hz), 3.12 (1H, dd, J=12.5 and 5.7Hz), 3.49-3.62 (1H, m), 4.21 (1H, t, J=6.6Hz), 4.38 (2H, d, J=6.6Hz), 4.65-4,80 (1H, m), 5.71 (1H, d, J=9.2Hz), 7.12-7.46 (9H, m), 7.59 (2H, t, J=7.0Hz), 7.77 (2H, d, J=7.4Hz); MASS (ES+): m/e 485.13 (M+1).

Preparation 67

A solution of piperidine in N,N-dimethylformamide (20% v/v, 20 ml) was added to the Compound (66) (1.6 g), and the resulting suspension was shaken using rotary shaker for 15 minutes. The suspension was filtered and then 20% N,N-dimethylformamide solution of piperidine (15 ml) was added to the residual solid and the suspension was shaken for additional 15 minutes. The

suspension was filtered and the residual solid was washed with N,N-dimethylformamide (20 ml, 3 times). To the solid were added (S)-6-benzoyloxy-2-N-tert-butoxycarbonylaminohexanoic acid (1.53 g), benzotriazole-1-yloxy-tris-pyrrolidinephoponium hexafluorophosphate (PyBOP®; 2.34 g) and N,N-diisopropylethylamine (581 mg) at ambient temperature and the resulting suspension was shaken at the same temperature for 16 hours. The suspension was filtered and the residual solid was washed with N,N-dimethylformamide (10 ml, twice), isopropyl alcohol (10 ml), dichloromethane (10 ml, twice). This washing cycle was repeated once and then the solid was washed with isopropyl alcohol (10 ml) and diethyl ether (10 ml) successively, and dried to give Compound (67) (1.80 g).

To determine the loading value, the Compound (67) (300 mg) was treated with a mixture of dichloromethane-trifluoroacetic acid (1:1 v/v, 4 ml) for 1 hour. The Compound (67) was filtered and the filtrate was concentrated in vacuo and the residual solvent was removed azeotropically with toluene to give a tripeptide compound. The purity of the tripeptide compound was determined by HPLC analysis. Mightysil RP-18 GP 250-4.6 (5 mm) (Kanto chemical Co., Ltd.), 0.1% TFA-acetonitrile/0.1% TFA-water 40:60 rt=7.76 minutes.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.66-0.83 (3H, m), 1.19-2.38 (9H, m), 2.68-2.85 (1H, m), 2.91-3.12 (2H, m), 3.58-3.74 (1H, m), 4.11-4.25 (1H, m), 4.30-4.46 (3H, m), 4.98 (1H, br.s), 5.71 (1H, br. s), 7.11-7.52 (10H, m), 7.60 (2H, d, J=6.9Hz), 7.76 (2H, d, J=7.3Hz);

MASS (ES+): m/e 584.39 (M+1).

Preparation 68

A solution of piperidine in N,N-dimethylformamide (20% v/v, 100 ml) was added to the Compound (67) (1.15 g) and the suspension was shaken using rotary shaker for 15 minutes. The suspension was filtered, then a solution of piperidine in N,N-dimethylformamide (20% v/v, 100 ml) was added to the residual solid, and the suspension was shaken for additional 15 minutes. The suspension was filtered and washed with N,N-dimethylformamide (15 ml, 5 times). To the residual solid were added Compound (5) (1.15 g), benzotriazole-1-yloxy-tris-pyrrolidinephoponium hexafluorophosphate (PyBOP®; 1.69 g) and N,N-

diisopropylethylamine (420 mg) at ambient temperature and the resulting suspension was shaken at the same temperature for 36 hours. The suspension was filtered and the residual solid was washed with N,N-dimethylformamide (10 ml, twice), isopropyl alcohol (10 ml), dichloromethane (10 ml, twice). This washing cycle was repeated and then the residual solid was washed with isopropyl alcohol (10 ml) and diethyl ether (20 ml) successively to give Compound (68) (300 mg).

Preparation 69

The Compound (68) (300 mg) was treated with a mixture of dichloromethane-trifluoroacetic acid (1:1 v/v, 6 ml) for 1 hour. The suspension was filtered and the filtrate was concentrated in vacuo to give Compound (69) (128 mg). The purity of the Compound B1-5 was determined by HPLC analysis. Mightysil RP-18 GP 250-4.6 (5 mm) (Kanto chemical Co., Ltd.), 0.1% TFA-acetonitrile/0.1% TFA-water 40:60 rt=7.76 minutes. The Compound (69) was used in Preparation 103.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.69 (3H, t, J=6.8Hz), 1.28 (3H, s), 1.46-1.70 (3H, m), 1.71-2.08 (9H, m), 2.84-3.04 (3H, m), 3.63-3.78 (1H, m), 4.04-4.15 (1H, m), 4.20-4.38 (3H, m), 4.79-4.90 (1H, m), 7.11-7.32 (6H, m), 7.41 (2H, t, J=8.1Hz), 7.45-7.62 (2H, m), 7.73-8.14 (5H, m);

MASS (ES+); m/e 595.21 (M+1).

Preparation 70

Compound (70) was obtained in a manner similar to Preparations 68.

Preparation 71

Compound (71) was obtained in a manner similar to Preparation 69. The obtained compound was used in Preparation 97.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.67 (3H, t, J=7.3Hz), 1.29 (3H, s), 1.51-1.63 (2H, m), 1.63-2.06 (10H, m), 2.36 (3H, s), 2.83-3.0 (2H, m), 3.0-3.15 (1H, m), 3.68-3.78 (1H, m), 4.0-4.10 (1H, m), 4.26-4.40 (3H, m), 4.84 (1H, m), 5.20-5.45 (1H, brs), 7.10-7.32 (4H, m), 7.41 (2H, t, J=7.6Hz), 7.52 (1H, t, J=7.3Hz), 7.66 (1H, brd, J=3.3Hz), 7.80-8.10 (1H, brs), 7.99 (2H, d, J=6.9Hz).

Preparation 72

Compound (72) was obtained in a manner similar to Preparation 69. The obtained compound was used in Preparation 82.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.69 (3H, t, J=7.3Hz), 1.32 (3H, s),

1.46-2.24 (12H, m), 2.81-3.11 (3H, m), 3.65-3.79 (1H, m), 3.97-4.58 (4H, m), 4.82-4.95 (1H, m), 6.95 (2H, t, J=8.8Hz), 7.11-7.31 (4H, m), 7.36-7.82 (4H, m), 7.99 (2H, d, J=7.0Hz), 8.04 (1H, br.s);

MASS (ES+): m/e 613.21 (M+1, free).

Preparation 73

Compound (73) was obtained in a manner similar to Preparations 68. The obtained compound was used in Preparation 109.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.70 (3H, t, J=7.4Hz), 1.29 (3H, s), 1.44-2.11 (12H, m), 2.80-3.03 (3H, m), 3.63-3.78 (1H, m), 3.76 (3H, s), 4.02-4.46 (4H, m), 4.75-4.88 (1H, m), 6.79 (2H, d, J=8.3Hz), 7.09 (2H, d, J=8.3Hz), 7.14-7.31 (2H, m), 7.36-7.80 (4H, m), 8.00 (2H, d, J=7.4Hz), 8.13 (1H, br. s);

MASS (ES+): m/e 625.28 (M+1, free).

Preparation 74

Compound (74) was obtained in a manner similar to Preparations 68. The obtained compound was used in Preparation 106.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.58-0.94 (6H, m), 0.95-1.33 (2H, m), 1.49-2.16 (16H, m), 3.00 (2H, br. d, J=8.1Hz), 3.03-3.18 (1H, m), 3.68-3.87 (1H, m), 4.02-4.16 (1H, m), 4.19-4.38 (3H, m), 4.67-4.83 (1H, m), 4.73-5.16 (2H, m), 7.11-7.35 (5H, m), 7.36-7.84 (4H, m), 7.94-8.19 (1H, br. s), 7.97-8.04 (2H, m);

MASS (ES+): m/e 637.23 (M+1, free).

Preparation 75

Compound (75) was obtained in a manner similar to Preparation 68. The obtained compound was used in Preparation 100.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.48 (3H, t, J=7.3Hz), 0.64 (3H, t, J=7.2Hz), 0.72-0.91 (2H, m), 1.52-2.17 (12H, m), 2.91-3.11 (3H, m), 3.70-3.83 (1H, m), 3.97-4.43 (4H, m), 4.74-5.03 (1H, m), 7.13-7.34 (5H, m), 7.37-7.72 (4H, m), 7.76-7.84 (1H, m), 7.95-8.18 (2H, m), 7.97-8.04 (2H, m).

Preparation 76

To a stirred solution of benzotriazol-1-yl-oxy-tris-(N,N-dimethylamino)phosphoniumhexafluorophosphate (23.9 g) and 4-(N,N-dimethylamino)pyridine (7.6 g) in dry N,N-dimethylformamide (1.5 L), the Compound (18) (4.64 g) in dry N,N-dimethylformamide (8 ml) was added dropwise over 20 hours at room temperature. The

volatiles were removed under reduced pressure and the residue was diluted with ethyl acetate (300 ml). The precipitate formed was collected by filtration, dissolved in ethyl acetate (50 ml), then washed with 5% aqueous potassium hydrogen sulfate solution (100 ml, 4 times), saturated aqueous sodium bicarbonate solution (100 ml, 3 times), water (100 ml) and brine (100 ml). The organic layer was dried over anhydrous magnesium sulfate and filtered. The filtrate was concentrated under reduced pressure and the residue was purified by flash column chromatography (eluted with ethyl acetate/hexane = 1:1 v/v) to give Compound (76) (3.083 g) as a colorless amorphous.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.83 (3H, t, J=7.0Hz), 1.28 (3H, s), 1.36-1.55 (2H, m), 1.59-1.99 (4H, m), 2.04-2.24 (2H, m), 2.24-2.40 (2H, m), 2.90 (1H, dd, J=13.6, 6.6Hz), 3.19 (1H, dd, J=13.6, 9.9Hz), 3.20-3.31 (1H, m), 3.80-3.91 (1H, m), 4.18-4.28 (1H, m), 4.32 (2H, t, J=6.2Hz), 4.67 (1H, br-d, J=5.5Hz), 5.03 (2H, s), 5.14 (1H, dt, J=10 and 5.6Hz), 5.85 (1H, s), 6.89 (2H, d, J=8.6Hz), 7.14 (1H, s), 7.15 (2H, d, J=8.6Hz), 7.28-7.48 (9H, m), 7.49-7.60 (2H, m), 8.00-8.06 (2H, m);

MASS (ES+): m/e 683.49 (M+1).

Preparation 77

To a stirred solution of the Compound (76) (3.07 g) in methanol (30 ml) was added 1N aqueous sodium hydroxide solution (11.2 ml, 2.5 eq) under ice-cooling and the mixture was stirred at ambient temperature for 4 hours. The pH of the mixture was adjusted to pH 7 with 1N hydrogen chloride, then methanol was evaporated under reduced pressure. The residue was extracted with ethyl acetate (300 ml). The organic layer was washed with saturated aqueous ammonium chloride (50 ml, twice), water (50 ml) and brine (50 ml), dried over sodium sulfate and filtered. The filtrate was concentrated in vacuo and the residue was purified by flash column chromatography (ethyl acetate, then methanol/ethyl acetate = 5:95 v/v) to give Compound (77) (2.63 g) as a colorless amorphous solid.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (3H, t, J=7.4Hz), 1.28 (3H, s), 1.20-1.92 (8H, m), 2,07-2.23 (2H, m), 2,24-2,39 (2H ,m), 2.89 (1H, dd, J=13.8 and 6.1Hz), 3.18 (1H, dd, J=13.8 and 9.5Hz), 3.15-3.28 (1H. m), 3.65 (2H, d, J=6.5Hz), 3.78-3.91 (1H, m), 4.15-4.28 (1H, m), 4.67 (1H, br-d, J=5.8Hz), 5.03 (2H ,s), 5.13 (1H, dt, J=9.5

and 6.2Hz), 5.93 (1H, s), 6.88 (2H, d, J=8.5Hz), 7.11-7.15 (1H, m), 7.14 (2H, d, J=8.5Hz), 7.27-7.45 (5H, m), 7.52 (1H, d, J=10.2Hz);

MASS (ES+): m/e 579.30 (M+1).

Preparation 78

To a stirred solution of the Compound (77) (1.0 g) in dichloromethane (50 ml) was added 1,1,1-triacetoxy-1,1-dihydro-1,2-benziodoxol-3(1H)-one (Dess-Martin periodinane) (3.66 g) in one portion under ice-cooling. The mixture was stirred at ambient temperature for 2 hours. The reaction was quenched with a solution of 20% sodium thiosulfate in saturated sodium hydrogen carbonate (100 ml) under ice-cooling, then the mixture was extracted with ethyl acetate (100 ml), washed with saturated aqueous sodium bicarbonate, water and brine, dried over sodium sulfate, and evaporated in vacuo to give Compound (78) as a colorless amorphous (980 mg). The obtained compound was used in Example 1.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (3H, t, J=7.3Hz), 1.30 (3H, s), 1.50-1.91 (6H, m), 2.08-2.38 (4H, m), 2.46-2.55 (2H, br-t, J=6.8Hz), 2.90 (1H, dd, J=13.7 and 5.9Hz), 3.18 (1H, dd, J=13.7 and 7.3Hz), 3.20-3.30 (1H, m), 3.80-3.91 (1H, m), 4.17-4.29 (1H, m), 4.68 (1H, br-d, J=6.3Hz), 5.03 (2H, s), 5.14 (1H, dt, J=9.5 and 5.6Hz), 5.90 (1H, s), 6.89 (2H ,d, J=8.5Hz), 7.10-7.21 (1H, m), 7.14 (2H, d, J=8.5Hz), 7.22-7.45 (5H, m), 7.47 (1H, d, J=10.3Hz), 9.77 (1H, s);

MASS (ES+): m/e 577.25 (M+1).

Preparation 79

Compound (79) was obtained in a manner similar to Preparation 76.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.83 (3H, t, J=7.3Hz), 1.28 (3H, s), 1.46 (2H, m), 1.60-1.98 (6H, m), 2.06-2.40 (4H, m), 2.90 (1H, dd, J=14 and 6Hz), 3.18 (1H, dd, J=14 and 10Hz), 3.26 (1H, m), 3.77 (3H, s), 3.86 (1H, m), 4.24 (1H, m), 4.32 (2H, t, J=6.5Hz), 4.67 (1H, m), 5.14 (1H, ddd, J=10, 10 and 6Hz), 5.85 (1H, s), 6.81 (2x1H, d, J=9Hz), 7.14 (2x1H, d, J=9Hz), 7.14 (1H, d, J=10Hz), 7.44 (2x1H, dd, J=7.5 and 7.5Hz), 7.50-7.60 (2H, m), 8.03 (2x1H, d, J=7.5Hz);

MASS (ES-): m/e 605.

Preparation 80

Compound (80) was obtained in a manner similar to Preparation 77.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (3H, t, J=7.3Hz), 1.25-1.51 (2H, m), 1.28 (3H, s), 1.54-1.94 (6H, m), 2.08-2.40 (4H, m), 2.89 (1H, dd, J=13.5 and 6Hz), 3.18 (1H, dd, J=13.5 and 10Hz), 3.25 (1H, m), 3.65 (2H, m), 3.77 (3H, s), 3.85 (1H, m), 4.22 (1H, dt, J=10 and 7.5Hz), 4.67 (1H, m), 5.13 (1H, ddd, J=10, 10 and 6Hz), 5.99 (1H, s), 6.81 (2x1H, d, J=8.7Hz), 7.14 (2x1H, d, J=8.7Hz), 7.15 (1H, d, J=10Hz), 7.53 (1H, d, J=10Hz);

MASS (ES-): m/e 501.

Preparation 81

Compound (81) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 2.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.85 (3H, t, J=7.3Hz), 1.29 (3H, s), 1.53-1.90 (6H, m), 2.08-2.37 (4H, m), 2.50 (2H, m), 2.89 (1H, dd, J=14 and 6Hz), 3.17 (1H, dd, J=14 and 10Hz), 3.25 (1H, m), 3.86 (1H, m), 4.23 (1H, m), 4.67 (1H, m), 5.13 (1H, ddd, J=10, 10 and 6Hz), 5.89 (1H, s), 6.81 (2x1H, d, J=8.8Hz), 7.14 (2x1H, d, J=8.8Hz), 7.16 (1H, d, J=11Hz), 7.48 (1H, d, J=10Hz), 9.77 (1H, t, J=1.4Hz);

MASS (ES-): m/e 499.

Preparation 82

Compound (82) was obtained in a manner similar to Preparation 76.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.81 (3H, t, J=7.3Hz), 1.27 (3H, s), 1.35-1.98 (8H, m), 2.06-2.40 (4H, m), 2.93 (1H, dd, J=13.6, 6.8Hz), 3.20 (1H, dd, J=13.6 and 9.6Hz), 3.21-3.33 (1H, m), 3.78-3.90 (1H, m), 4.18-4.30 (1H, m), 4.32 (2H, t, J=6.4Hz), 4.68 (1H, br. d, J=7.7Hz), 5.07-5.20 (1H, m), 5.84 (1H, s), 6.96 (2H, t, J=8.6Hz), 7.10 (1H, d, J=10.3Hz), 7.19 (1H, dd, J=8.6 and 5.5Hz), 7.44 (2H, t, J=7.3Hz), 7.52-7.61 (2H, m), 8.03 (2H, d, J=8.4Hz);

MASS (ES+): m/e 595.39 (M+1).

Preparation 83

Compound (83) was obtained in a manner similar to Preparation 77.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (3H, t, J=7.3Hz), 1.23-1.95 (8H, m), 1.29 (3H, s), 2.08-2.41 (4H, m), 2.94 (1H, dd, J=13.6 and 6.2Hz), 3.21 (1H, dd, J=13.6 and 9.6Hz), 3.23-3.33 (1H, m), 3.67 (2H, br. t, J=6.2Hz), 3.80-3.91 (1H, m), 4.16-4.30 (1H, m), 4.69

(1H br. d, J=5.5Hz), 5.07-5.20 (1H, m), 5.97 (1H, s), 6.97 (2H, t, J=8.5Hz), 7.11 (1H, d, J=10.2Hz), 7.20 (2H, dd, J=8.5 and 5.1Hz), 7.57 (1H, d, J=10.2Hz);

MASS (ES+): m/e 491.45 (M+1).

Preparation 84

Compound (84) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 3.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.83 (3H, t, J=6.9Hz), 1.29 (3H, s), 1.53-1.90 (6H, m), 2.08-2.38 (4H, m), 2.50 (2H, br. t, J=7.0Hz), 2.93 (1H, dd, J=13.9 and 6.2Hz), 3.19 (1H, dd, J=13.9 and 9.1Hz), 3.20-3.31 (1H, m), 3.79-3.90 (1H, m), 4.17-4.28 (1H, m), 4.68 (1H, br. d, J=6.0Hz), 5.07-5.19 (1H, m), 5.87 (1H, s), 6.96 (2H, t, J=8.9Hz), 7.10 (1H, d, J=10.1Hz), 7.19 (2H, dd, J=8.9 and 5.5Hz), 7.50 (1H, d, J=10.3Hz), 9.77 (1H, s);

MASS (ES+): m/e 489.42 (M+1).

Preparation 85

Compound (85) was obtained in a manner similar to Preparation 76.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.31-1.96 (14H, m), 2.08-2.23 (1H, m), 2.24-2.37 (2H, m), 2.43-2.56 (2H, m), 2.95 (1H, dd, J=13.5 and 5.7Hz), 3.14-3.28 (1H, m), 3.26 (1H, dd, J=13.5 and 10.5Hz), 3.84-3.95 (1H, m), 4.23 (1H, dt, J=10.2 and 7.8Hz), 4.31 (2H, t, J=6.6Hz), 4.63-4.69 (1H, m), 5.15 (1H, ddd, J=10.2, 10.2 and 6.0Hz), 6.13 (1H, s), 7.16-7.31 (6H, m), 7.39-7.48 (3H, m), 7.52-7.60 (1H, m), 8.00-8.05 (2H, m);

MASS (ES+): m/e 589.40 (M+1).

Preparation 86

Compound (86) was obtained in a manner similar to Preparation 77.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.20-1.81 (14H, m), 2.10-2.22 (1H, m), 2.25-2.37 (2H, m), 2.43-2.58 (2H, m), 2.95 (1H, dd, J=13.5 and 5.7Hz), 3.13-3.28 (1H, m), 3.25 (1H, dd, J=13.5 and 10.2Hz), 3.65 (2H, t, J=6.3Hz), 3.85-3.95 (1H, m), 4.22 (1H, dt, J=10.2 and 7.2Hz), 4.67 (1H, dd, J=7.8 and 2.1Hz), 5.15 (1H, ddd, J=10.2, 10.2 and 6.0Hz), 6.28 (1H, s), 7.16-7.31 (6H, m), 7.44 (1H, d, J=10.2Hz);

MASS (ES+): m/e 485.39 (M+1).

Preparation 87

Compound (87) was obtained in a manner similar to

Preparation 78. The obtained compound was used in Example 4. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.42-1.92 (13H, m), 2.08-2.22 (1H, m), 2.23-2.37 (2H, m), 2.42-2.56 (2H, m), 2.95 (1H, dd, J=13.8 and 5.7Hz), 3.13-3.28 (1H, m), 3.25 (1H, dd, J=13.8 and 10.2Hz), 3.85-3.95 (1H, m), 4.22 (1H, dt, J=10.2 and 7.2Hz), 4.64-4.69 (1H, m), 5.15 (1H, ddd, J=9.9, 9.9 and 5.7Hz), 6.15 (1H, s), 7.17-7.31 (6H, m), 7.44 (1H, d, J=10.2Hz), 9.77 (1H, s);
MASS (ES+): m/e 483.36 (M+1).

Preparation 88

Compound (88) was obtained in a manner similar to Preparation 76.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.790 (3H, t, J=7.2Hz), 1.27 (3H, s), 1.38-1.98 (8H, m), 2.07-2.38 (4H, m), 3.06 (1H, dd, J=14.1 and 6.9Hz), 3.28-3.36 (1H, m), 3.26 (1H, dd, J=14.1 and 8.4Hz), 3.79-3.89 (1H, m), 4.25 (1H, dt, J=10.2 and 7.8Hz), 4.32 (2H, t, J=6.3Hz), 4.65-4.71 (1H, m), 5.17 (1H, dt, J=9.0 and 6.9Hz), 5.89 (1H, s), 7.01 (1H, d, J=10.2Hz), 7.32-7.38 (2H, m), 7.40-7.48 (2H, m), 7.52-7.63 (3H, m), 7.61-7.67 (1H, m), 8.00-8.06 (2H, m);
MASS (ES+): m/e 602.47 (M+1).

Preparation 89

Compound (89) was obtained in a manner similar to Preparation 77.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.809 (3H, t, J=7.2Hz), 1.24-1.94 (9H, m), 1.28 (3H, s), 2.06-2.41 (4H, m), 3.06 (1H, dd, J=9.0 and 6.9Hz), 3.26-3.36 (1H, m), 3.26 (1H, dd, J=13.5 and 9.0Hz), 3.66 (2H, t, J=6.3Hz), 3.79-3.90 (1H, m), 4.24 (1H, dt, J=10.2 and 7.8Hz), 4.65-4.72 (1H, m), 5.18 (1H, dt, J=9.0 and 7.2Hz), 6.01 (1H, s), 7.02 (1H, d, J=10.2Hz), 7.35 (2H, d, J=8.1Hz), 7.58 (2H, d, J=8.1Hz), 7.64 (1H, d, J=10.2Hz);
MASS (ES+): m/e 498.41 (M+1).

Preparation 90

Compound (90) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 5.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.812 (3H, t, J=7.2Hz), 1.29 (3H, s), 1.49-1.92 (6H, m), 2.07-2.40 (4H, m), 2.51 (2H, t, J=7.2Hz), 3.06 (1H, dd, J=13.5 and 6.9Hz), 3.26-3.36 (1H, m), 3.26 (1H, dd, J=13.5 and 8.7Hz), 3.78-3.90 (1H, m), 4.24 (1H, dt, J=10.2 and 7.2Hz), 4.65-4.71 (1H, m), 5.18 (1H, dt, J=9.0 and 8.4Hz), 5.93 (1H, s), 7.02 (1H, d, J=10.2Hz), 7.35 (2H, d, J=8.7Hz), 7.57-7.59

(1H, m), 7.58 (2H, d, J=8.8Hz), 9.77 (1H, s);
MASS (ES+): m/e 496.46 (M+1).

Preparation 91

Compound (91) was obtained in a manner similar to Preparation 76.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.82 (3H, t, J=7.5Hz), 1.27 (3H, s), 1.39 (3H, t, J=7.2Hz), 1.40-1.52 (2H, m), 1.64-1.98 (6H, m), 2.06-2.39 (4H, m), 2.88 (1H, dd, J=13.5 and 5.7Hz), 3.09-3.32 (2H, m), 3.79-3.90 (1H, m), 3.99 (2H, q, J=7.2Hz), 4.18-4.30 (1H, m), 4.31 (2H, t, J=6.0Hz), 4.62-4.69 (1H, m), 5.07-5.18 (1H, dt, J=9.9 and 6.0Hz), 5.82 (1H, s), 6.79 (2H, d, J=8.4Hz), 7.10-7.18 (1H, m), 7.13 (2H, d, J=8.4Hz), 7.38-7.59 (4H, m), 7.99-8.05 (2H, m);
MASS (ES+): m/e 621.55 (M+1).

Preparation 92

Compound (92) was obtained in a manner similar to Preparation 77.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (3H, t, J=7.2Hz), 1.28-1.93 (8H, m), 1.28 (3H, s), 1.39 (3H, t, J=6.9Hz), 2.08-2.23 (2H, m), 2.24-2.39 (2H, m), 2.88 (1H, dd, J=13.5 and 6.0Hz), 3.17 (1H, dd, J=13.5 and 9.9Hz), 3.20-3.30 (1H, m), 3.65 (2H, t, J=6.6Hz), 3.80-3.90 (1H, m), 3.99 (2H, q, J=6.9Hz), 4.22 (1H, dt, J=10.2 and 7.8Hz), 4.64-4.69 (1H, m), 5.13 (1H, dt, J=9.9 and 6.0Hz), 5.93 (1H, s), 6.79 (2H, d, J=8.4Hz), 7.10-7.17 (1H, m), 7.13 (2H, d, J=8.4Hz), 7.52 (1H, d, J=10.2Hz);
MASS (ES+): m/e 517.44 (M+1).

Preparation 93

Compound (93) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 6.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.85 (3H, t, J=7.2Hz), 1.29 (3H, s), 1.40 (3H, t, J=6.9Hz), 1.49-1.92 (6H, m), 2.09-2.24 (2H, m), 2.24-2.39 (2H, m), 2.50 (2H, dt, J=6.3 and 1.2Hz), 2.88 (1H, dd, J=14.1 and 5.7Hz), 3.17 (1H, dd, J=14.1 and 10.2Hz), 3.20-3.30 (1H, m), 3.81-3.90 (1H, m), 3.99 (2H, q, J=6.9Hz), 4.23 (1H, dt, J=10.2 and 7.2Hz), 4.64-4.70 (1H, m), 5.13 (1H, dt, J=10.2, 5.7Hz), 5.85 (1H, s), 6.80 (2H, d, J=8.4Hz), 7.12-7.19 (1H, m), 7.13 (2H, d, J=8.4Hz), 7.46 (1H, d, J=10.2Hz), 9.77 (1H, t, J=1.2Hz);
MASS (ES+): m/e 515.36 (M+1).

Preparation 94

Compound (94) was obtained in a manner similar to Preparation 76.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.78 (3H, t, J=7.5Hz), 1.25 (3H, s), 1.46 (2H, m), 1.58-1.95 (6H, m), 2.07-2.39 (4H, m), 3.11 (1H, dd, J=14 and 8Hz), 3.16 (1H, dd, J=14 and 8Hz), 3.41 (1H, m), 3.88 (1H, m), 4.24 (1H, m), 4.32 (2H, t, J=6.5Hz), 4.70 (1H, dd, J=8 and 3Hz), 5.24 (1H, ddd, J=10, 8 and 8Hz), 5.80 (1H, s), 6.97-7.31 (5H, m), 7.44 (2H, dd, J=7.5 and 7.5Hz), 7.50-7.60 (2H, m), 8.00-8.06 (2H, m);
MASS (ES+): m/e 595;
MASS (ES-): m/e 593.

Preparation 95

Compound (95) was obtained in a manner similar to Preparation 77.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.79 (3H, t, J=7.5Hz), 1.22-1.51 (2H, m), 1.26 (3H, s), 1.52-1.73 (3H, m), 1.74-1.94 (3H, m), 2.08-2.40 (4H, m), 3.10 (1H, dd, J=15 and 8Hz), 3.15 (1H, dd, J=15 and 8Hz), 3.41 (1H, m), 3.66 (2H, t, J=7Hz), 3.88 (1H, m), 4.23 (1H, m), 4.70 (1H, m), 5.24 (1H, ddd, J=10, 8 and 8Hz), 5.91 (1H, s), 6.97-7.08 (2H, m), 7.10 (1H, d, J=10Hz), 7.15-7.28 (2H, m), 7.54 (1H, d, J=10Hz);
MASS (ES+): m/e 491;
MASS (ES-): m/e 489.

Preparation 96

Compound (96) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 7.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.80 (3H, t, J=7Hz), 1.26 (3H, s), 1.50-1.94 (6H, m), 2.11-2.44 (4H, m), 2.51 (2H, m), 3.05-3.20 (2H, m), 3.41 (1H, m), 3.89 (1H, m), 4.24 (1H, m), 4.71 (1H, m), 5.24 (1H, m), 5.85 (1H, s), 6.97-7.28 (5H, m), 7.49 (1H, d, J=10Hz), 9.78 (1H, s);
MASS (ES-): m/e 487;
MASS (ES+): m/e 489.

Preparation 97

Compound (97) was obtained in a manner similar to Preparation 76.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.83 (3H, t, J=7.3Hz), 1.28 (3H, s), 1.25-1.47 (2H, m), 1.56-1.74 (4H, m), 1.76-1.89 (2H, m), 2.15-

2.36 (4H, m), 2.93 (1H, dd, J=13.6 and 6.6Hz), 3.20 (1H, dd, J=13.6 and 9.5Hz), 3.20-3.32 (1H, m), 3.66 (2H, t, J=6.6Hz), 3.85 (1H, ddd, J=13.2, 8.1 and 4.4Hz), 4.22 (1H, ddd, J=15, 7.6 and 2.2Hz), 4.67 (1H, brd, J=5.8Hz), 5.15 (1H, ddd, J=16.5, 9.5 and 6.6Hz), 5.99 (1H, s), 7.08 (1H, d, J=10.6Hz), 7.16 (2H, d, J=8.9Hz), 7.22 (2H, d, J=8.9Hz), 7.58 (1H, d, J=10.3Hz).

<u>Preparation 98</u>

Compound (98) was obtained in a manner similar to Preparation 77.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.81 (3H, t, J=7.3Hz), 1.27 (3H, s), 1.41-1.58 (2H, m), 1.61 (3H, s), 1.71-1.90 (4H, m), 2.05-2.34 (4H, m), 2.95 (1H, dd, J=13.5 and 6.2Hz), 3.20 (1H, dd, J=13.5 and 9.2Hz), 3.25-3.36 (1H, m), 3.82-3.89 (1H, m), 4.25 (1H, dd, J=17.9 and 10.2Hz), 4.32 (2H, t, J=6.2Hz), 4.68 (1H, brd, J=6.6Hz), 5.14 (1H, ddd, J=16.7, 9.5 and 6.6Hz), 5.81 (1H, s), 7.08 (1H, d, J=9.9Hz), 7.16 (2H, d, J=8.1Hz), 7.24 (2H, d, J=8.1Hz), 7.44 (2H, t, J=8.4Hz), 7.56 (1H, dd, J=6.6 and 4.3Hz), 8.03 (2H, d, J=7.3Hz).

<u>Preparation 99</u>

Compound (99) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 8.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.83 (3H, t, J=7.5Hz), 1.29 (3H, s), 1.52-1.90 (6H, m), 2.08-2.38 (4H, m), 2.50 (2H, m), 2.94 (1H, dd, J=13.5 and 6Hz), 3.19 (1H, dd, J=13.5 and 9.5Hz), 3.28 (1H, m), 3.85 (1H, m), 4.24 (1H, m), 4.68 (1H, m), 5.14 (1H, ddd, J=10, 9.5 and 6Hz), 5.89 (1H, s), 7.09 (1H, d, J=10.5Hz), 7.16 (2X1H, d, J=8.5Hz), 7.25 (2X1H, d, J=8.5Hz), 7.52 (1H, d, J=10Hz), 9.77 (1H, t, J=1.3Hz);

MASS (ES-): m/e 503.

<u>Preparation 100</u>

Compound (100) was obtained in a manner similar to Preparation 76.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.75 (3H, t, J=7.3Hz), 0.91 (3H, t, J=7.3Hz), 1.35-1.98 (10H, m), 2.10-2.43 (4H, m), 2.97 (1H, dd, J=13.5 and 6.4Hz), 3.24 (1H, dd, J=13.5 and 9.4Hz), 3.21-3.30 (1H, m), 3.83-3.94 (1H, m), 4.25 (1H, dt, J=10.3 and 7.6Hz), 4.32 (2H, t, J=6.2Hz), 4.63-4.70 (1H, m), 5.18 (1H, dt, J=10.2 and 6.3Hz), 5.78 (1H, s), 7.13 (1H, d, J=10.3Hz), 7.19-7.32 (5H, m), 7.40-7.47 (2H, m), 7.50 (1H, d, J=10.2Hz), 7.51-7.60 (1H, m), 8.01-

8.06 (2H, m);
MASS (ES+): m/e 591.21 (M+1).

Preparation 101

Compound (101) was obtained in a manner similar to Preparation 77.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.77 (3H, t, J=7.7Hz), 0.91 (3H, t, J=7.3Hz), 1.20-1.93 (10H, m), 2.07-2.45 (4H, m), 2.97 (1H, dd, J=13.5 and 6.2Hz), 3.24 (1H, dd, J=13.5 and 9.1Hz), 3.21-3.30 (1H, m), 3.66 (2H, t, J=6.6Hz), 3.82-3.93 (1H, m), 4.24 (1H, dd, J=10.0 and 7.2Hz), 4.67 (1H, br. d, J=8.0Hz), 5.12-5.23 (1H, m), 5.84 (1H, s), 7.12 (1H, d, J=10.0Hz), 17.16-7.31 (5H, m), 7.49 (1H, d, J=10.4Hz);
MASS (ES+): m/e 487.19 (M+1).

Preparation 102

Compound (102) was obtained in a manner similar to preparation 78. The obtained compound was used in Example 9.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.77 (3H, t, J=7.4Hz), 0.91 (3H, t, J=7.4Hz), 1.50-1.92 (8H, m), 2.07-2.42 (4H, m), 2.51 (2H, br. t, J=6.1Hz), 2.96 (1H, dd, J=13.1 and 5.7Hz), 3.17-3.30 (2H, m), 3.83-3.94 (1H, m), 4.18-4.30 (1H, m), 4.67 (1H, br. d, J=6.1Hz), 5.12-5.23 (1H, m), 5.85 (1H, s), 7.15 (1H, d, J=10.8Hz), 7.18-7.31 (5H, m), 7.44 (1H, d, J=10.0Hz), 9.77 (1H, s);
MASS (ES+): m/e 485.29 (M+1).

Preparation 103

Compound (103) was obtained in a manner similar to Preparation 76 except that benzotriazol-1-yloxy-tris-pyrrolidinephoponium hexafluorophosphate was used instead of benzotriazol-1-yl-oxy-tris-(dimethylamino)phosphonium hexafluorophosphate.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.81 (3H, t, J=7.3Hz), 1.28 (3H, s), 1.46 (2H, m), 1.61-2.00 (6H, m), 2.06-2.39 (4H, m), 2.97 (1H, dd, J=13.5 and 6Hz), 3.24 (1H, dd, J=13.5 and 9.5Hz), 3.26 (1H, m), 3.86 (1H, m), 4.24 (1H, m), 4.32 (2H, t, J=6.5Hz), 4.67 (1H, m), 5.18 (1H, m), 5.82 (1H, s), 7.13 (1H, d, J=11Hz), 7.16-7.32 (5H, m), 7.39-7.59 (2H, m), 7.51-7.60 (2H, m), 7.95-8.08 (2H, m);
MASS (ES-): m/e 575.

Preparation 104

Compound (104) was obtained in a manner similar to Preparation 77.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.83 (3H, t, J=7.5Hz), 1.22-1.95 (8H, m), 1.28 (3H, s), 2.07-2.40 (4H, m), 2.96 (1H, dd, J=13 and 6.5Hz), 3.04 (1H, dd, J=13 and 9Hz), 3.06 (1H, m), 3.65 (2H, br-t, J=6Hz), 3.86 (1H, m), 4.23 (1H, m), 4.68 (1H, m), 5.19 (1H, ddd, J=10, 9, 6Hz), 5.93 (1H, s), 7.12 (1H, d, J=11Hz), 7.16-7.32 (5H, m), 7.55 (1H, d, J=10Hz);

MASS (ES-): m/e 471.

<u>Preparation 105</u>

Compound (105) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 10.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (3H, t, J=7.3Hz), 1.29 (3H, s), 1.48-1.95 (6H, m), 2.06-2.59 (6H, m), 2.97 (1H, dd, J=13.5 and 6Hz), 3.24 (1H, dd, J=13.5 and 10Hz), 3.26 (1H, m), 3.86 (1H, m), 4.24 (1H, m), 4.68 (1H, dd, J=8 and 2Hz), 5.19 (1H, ddd, J=10, 10 and 6Hz), 5.92 (1H, s), 7.16 (1H, d, J=11Hz), 7.16-7.33 (5H, m), 7.50 (1H, d, J=10Hz), 9.77 (1H, br-s);

MASS (ES-): m/e 469.

<u>Preparation 106</u>

Compound (106) was obtained in a manner similar to Preparation 76.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.87 (3H, t, J=7.2Hz), 0.96 (3H, t, J=7.0Hz), 0.93-1.04 (1H, m), 1.11-1.36 (3H, m), 1.37-1.64 (3H, m), 1.65-1.96 (7H, m), 2.00-2.24 (2H, m), 2.27-2.42 (2H, m), 2.98 (1H, dd, J=13.6 and 6.6Hz), 3.21-3.32 (1H, m), 3.23 (1H, dd, J=13.6 and 9.5Hz), 3.81-3.93 (1H, m), 4.18-4.29 (1H, m), 4.32 (2H, t, J=6.5Hz), 4.67 (1H, br. d, J=7.7Hz), 5.10-5.23 (1H, m), 5.78 (1H, s), 7.13 (1H, d, J=10.2Hz), 7.19-7.32 (5H, m), 7.40-7.60 (4H, m), 8.01-8.06 (2H, m);

MASS (ES+): m/e 619.34 (M+1).

<u>Preparation 107</u>

Compound (107) was obtained in a manner similar to Preparation 77.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.89 (3H, t, J=7.0Hz), 0.96 (3H, t, J=6.8Hz), 0.97-1.08 (1H, m), 1.12-1.92 (13H, m), 2.02-2.26 (2H, m), 2.27-2.44 (2H, m), 2.98 (1H, dd, J=13.5 and 6.6Hz), 3.20-3.31 (1H, m), 3.22 (1H, dd, J=13.5 and 9.6Hz), 3.66 (2H, br. t, J=6.3Hz), 3.82-3.92 (1H, m), 4.22 (1H, dt, J=10.2 and 7.6Hz), 4.67 (1H, br-d, J=7.5Hz), 5.11-5.22 (1H, m), 5.86 (1H, s), 7.12 (1H, d, J=10.3Hz), 7.17-7.31 (5H, m), 7.49 (1H, d, J=10.3Hz);

MASS (ES+): m/e 515.23 (M+1).

Preparation 108

Compound (108) was obtained in a manner similar to Preparation 78.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.89 (3H, t, J=6.6Hz), 0.94-1.08 (1H, m), 0.96 (3H, t, J=6.9Hz), 1.10-1.38 (4H, m), 1.43-1.92 (6H, m), 2.00-2.42 (5H, m), 2.50 (2H, br. t, J=6.6Hz), 2.98 (1H, dd J=13.5 and 6.6Hz), 3.20-3.31 (1H, m), 3.22 (1H, dd, J=13.5 and 9.2Hz), 3.81-3.92 (1H, m), 4.16-4.28 (1H, m), 4.67 (1H, J=5.8Hz), 5.10-5.22 (1H, m), 5.84 (1H, s), 7.14 (1H, d, J=10.3Hz), 7.15-7.32 (5H, m), 7.43 (1H, d, J=10.2Hz), 9.77 (1H, br. s);

MASS (ES+): m/e 513.26 (M+1).

Preparation 109

Compound (109) was obtained in a manner similar to Preparation 76.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.04 (3x3H, s), 1.26-1.40 (4H, m), 1.33 (3H, d, J=7Hz), 1.48-1.92 (6H, m), 2.16 (1H, m), 2.34 (1H, m), 2.54 (2H, m), 2.90 (1H, dd, J=13 and 5Hz), 3.02 (1H, m), 3.18 (1H, dd, J=13 and 10Hz), 3.90 (1H, m), 3.92 (1H, q, J=7Hz), 4.32 (1H, dt, J=10 and 7.5Hz), 4.49 (1H, d, J=12Hz), 4.55 (1H, d, J=12Hz), 4.59 (1H, m), 5.01 (1H, ddd, J=10, 10 and 5Hz), 6.21 (1H, d, J=10Hz), 6.23 (1H, d, J=10Hz), 7.13 (1H, d, J=10Hz), 7.16-7.41 (10H, m);

MASS (ES+): m/e 647.

Preparation 110

To a stirred solution of 2-indanone (12.5 g) in a mixture of ethanol (210 ml) and water (210 ml) was added sodium cyanide (11.6 g) and ammonium carbonate (100 g) at ambient temperature. The mixture was heated at 55 to 60°C for 6 hours and then allowed to cool to ambient temperature. The mixture was stirred at 0°C for half an hour and the precipitated solid was collected. The solid was recrystallized from ethanol to give 2-spirohydantoinindane (4.5 g).

^{1}H-NMR (300MHz, DMSO-d_6, δ): 3.04 (1H, s), 3.10 (1H, s), 3.22-3.42 (1H, br), 3.33 (1H, s), 3.38 (1H, s), 7.15-7.27 (4H, m), 10.25 (1H, brs);

MASS (ES+): m/e 202.18 (M).

Preparation 111

To a stirred solution of 2-spirohydantoinindane in

propylene glycol (13 ml) was added 40% aqueous solution of sodium hydoxide (22 ml) at ambient temperature. The mixture was refluxed for 24 hours. The reaction mixture was allowed to cool and then diluted with water (50 ml). After acidification with 1 N hydrochloric acid to pH 2, the precipitated solid was filtered and the filtrate was neutralized by addition of a 10% (w/v) sodium hydrogen carbonate solution. The mixture was stirred for an hour and left overnight at 0°C. Most of the solvent was removed under reduced pressure and the residue was stirred at 0°C. The precipitate were collected by filtration and recrystallyzed from ethanol/water to give 2-aminoindan-2-carboxylic acid (2.76 g) as a white-scaled crystal.

^{1}H-NMR (300MHz, D_2O, δ): 3.23 (1H, s), 3.29 (1H, s), 3.64 (1H, s), 3.70 (1H, s), 7.28-7.38 (4H, m);

MASS (ES+): m/e 178.00 (M+1).

Preparation 112

To a stirred solution of methyl (2R)-2-hydroxypropanoate (25 g) in N,N-dimethylformamide (250 ml) was added imidazole (66 g) followed by tert-butyldiphenylchlorosilane (68.08 g) at 0°C. The mixture was stirred at ambient temperature for two hours. The reaction mixture was poured into water and extracted with ethyl acetate. The organic layer was successively washed with water, 0.2 N hydrochloric acid, saturated sodium hydrogen carbonate and brine. The organic phase was dried over magnesium sulfate, filtered and evaporated to give methyl (2R)-2-tert-butyldiphenylsilylpropanoate (80.5 g) as a colorless oil.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.09 (9H, s), 1.37 (3H, d, J=6.9Hz), 3.56 (3H, s), 4.27 (1H, q, J=6.9 Hz), 7.32-7.48 (6H, m), 7.63-7.75 (4H, m);

MASS (ES+): m/e 375.29 (M+Na).

Preparation 113

To a stirred solution of dimethyl methylphosphonate (145 g) in tetrahydrofuran (750 ml) was added n-butyllithium (1.6 M in hexane, 127 ml) dropwise at -78°C over an hour and the resulting mixture was stirred at the same temperature for an hour. To this mixture was added dropwise a solution of methyl-(2R)-2-tert-butyldiphenylsilyloxypropanoate in tetrahydrofuran (450 ml) over an hour. The mixture was stirred at the same temperature for two hours, allowed to warm to -30°C over an hour and stirred at

ambient temperature for half an hour. The reaction mixture was poured into a stirred saturated ammonium chloride (2000 ml) in an ice bath and left at ambient temperature overnight. The aqueous phase was separated and extracted with ethyl acetate twice. The combined organic extracts were washed with water, brine and dried over magnesium sulfate. The organic phase was filtered and concentrated in vacuo. The crude product was purified by flash chromatography eluting with 33 to 60% ethyl acetate/hexane (v/v) to give dimethyl-(3R)-3-tert-buthyldiphenylsilyloxy-2-oxobutylphosphate (81.1 g) as a colorless oil.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.10 (9H, s), 2.21 (3H, d, J=6.9Hz), 3.08 (1H, dd, J=21.9, 15.0 Hz), 3.48 (1H, dd, J=20.4 and 15.0 Hz), 3.73 (3H, s), 3.77 (3H, s), 4.25 (3H, q, J=6.9 Hz), 7.33-7.49 (6H, m), 7.58-7.68 (4H, m);

MASS (ES+): m/e 435.31 (M+1).

Preparation 114

To a stirred solution of crude (2R)-2-aminobutanoic acid (12.1 g) in aqueous sulfuric acid (0.88 M, 200 ml) was added an aqueous sodium nitrite (8.8 M, 20 ml) dropwise at 0°C over two hours. The mixture was left at the same temperature and allowed to warm to ambient temperature. Additional concentrated sulfuric acid (10 ml) and aqueous sodium nitrite (12.1 g) were added at 0°C after thirteen hours and the mixture was left at ambient temperature for two days. Half of the volume of the solvent was evaporated under reduced pressure and the resulting solution was adjusted to pH 2 with sodium hydrogen carbonate. The resulting mixture was extracted twice with ethyl acetate. The combined organic extracts were washed with brine, dried over magnesium sulfate, filtered and evaporated carefully to give crude (2R)-2-hydroxybutanoic acid (6.57 g), which was used directly for the next step without further purification.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.03 (3H, t, J=7.5 Hz), 0.77 (1H, m), 1.90 (1H, m), 4.26 (1H, t, J=5 Hz);

MASS (ES-): m/e 103.

Preparation 115

To a stirred solution of crude (2R)-2-hydroxybutanoic acid (2.0 g) in a mixture of methanol (5 ml) and ether (15 ml) was added (trimethylsilyl)diazomethane (2.0 M in hexane, 9.6 ml) dropwise in an ice bath. The reaction mixture was stirred at

ambient temperature overnight. The solvent was evaporated carefully to give crude methyl (2R)-2-hydroxybutanoate as a pale yellow oil (1.9 g), which was used directly for the next step without further purification.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.96 (3H, t, J=7.5 Hz), 1.70 (1H, m), 1.84 (1H, m), 3.80 (3H, s), 4.17 (1H, dd, J=7.5 Hz);
MASS (ES+): m/e 119.

Preparation 116

To a stirred solution of methyl (2R)-2-hydroxybutanoate (1.74 g) in N,N-dimethylformamide (15 ml) was added a solution of tert-butyldiphenylchlorosilane (4.05 g) in N,N-dimethylformamide (5 ml) followed by imidazole (1.05 g) at ambient temperature. The resulting mixture was stirred at the same temperature for three hours and the reaction mixture was poured into ice water and extracted with ethyl acetate. The organic layer was washed with water, brine and dried over magnesium sulfate. The organic phase was filtered and concentrated in vacuo to give crude methyl-(2R)-2-tert-butyldiphenylsilyloxybutanoate (5.11 g), which was used directly for the next step without further purification.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.91 (3H, t, J=7.5 Hz), 1.10 (3X3H, s), 1.74 (2H, dq, J=7.5 and 5Hz), 3.48 (3H, s), 4.20 (1H, t, J=5Hz), 7.32-7.46 (6H, m), 7.59-7.75 (4H, m);
MASS (ES+) m/e 357.

Preparation 117

To a stirred solution of dimethyl methylphosphonate (8.87 g) in tetrahydrofuran (50 ml) was added n-butyllithium (1.6 M in hexane, 45 ml) dropwise at -78°C over twenty minutes and the resulting mixture was stirred at the same temperature for half an hour. To this was added a solution of methyl (2R)-2-tert-butyldiphenylsilyloxybutanoate in tetrahydrofuran (30 ml) dropwise at the same temperature over twenty minutes. The mixture was stirred at the same temperature for two hours and allowed to warm to 0°C. The reaction mixture was poured into saturated ammonium chloride and extracted twice with ethyl acetate. The combined organic extracts were washed twice with water, brine and dried over magnesium sulfate. The organic phase was filtered and concentrated in vacuo. The crude product was purified by flash chromatography eluting with 50% ethyl acetate /hexane (v/v) as a solvent mixture to give dimethyl (3R)-3-tert-

butyldiphenylsilyloxy-2-oxopentylphosphate (3.06 g) as a pale yellow oil.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.80 (3H, t, J=7.5Hz), 1.11 (3x3H, s), 1.63 (2H, m), 2.91 (1H, dd, J=22 and 16Hz), 3.35 (1H, dd, J=20 and 16Hz), 3.70 (3H, d, J=2Hz), 3.74 (3H, d, J=2Hz), 4.15 (1H, m), 7.32-7.48 (6H, m), 7.56-7.67 (4H, m);

MASS (ES+) m/e 447.

Preparation 118

Compound (118) was obtained in a manner similar to Preparation 1.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.41 (3x3H, s), 2.96 (2H, m), 4.50 (1H, m), 5.16 (1H, d, J=8.5Hz), 6.54 (1H, d, J=7.5Hz), 6.62-6.82 (2H, m);

MASS (ES-): m/e 296.

Preparation 119

To a stirred solution of (2S)-tert-butoxycarbonylamino-3-(3,4-dihydroxyphenyl)propanoic acid (13.66 g) in N,N-dimethylformamide (150 ml) was added potassium carbonate (22.9 g) at 0°C and the resulting mixture was stirred at the same temperature for half an hour. To this mixture was added methyl iodide (21.5 g) at the same temperature and the reaction mixture was left at ambient temperature for 2 days. The mixture was poured into water and extracted with ethyl acetate. The organic layer was washed with water, brine and dried over magnesium sulfate. The organic phase was filtered and concentrated in vacuo. The residue was purified by flash chlomatography eluting with 25 to 50% ethyl acetate/hexane (v/v) as a solvent mixture to give pure methyl (2S)-2-tert-butoxycarbonylamino-3-(3,4-dimethoxyphenyl)propanoate (7.17 g) as a brown oil.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.42 (3x3H, s), 3.01 (1H, dd, J=14 and 5.5Hz), 3.06 (1H, dd, J=14 and 5.5Hz), 3.72 (3H, s), 3.86 (2x3H, s), 4.56 (1H, ddd, J=8.5, 5.5 and 5.5Hz), 4.97 (1H, br-d, J=8.5Hz), 6.64 (1H, s), 6.66 (1H, d, J=8Hz), 6.79 (1H, d, J=8Hz);

MASS (ES+) m/e 340.

Preparation 120

To a stirred solution of methyl (2S)-2-tert-butoxycarbonylamino-3-(3,4-dimethoxyphenyl)propanoate (7.13 g) in methanol (40 ml) was added 1 N sodium hydroxide (40 ml) at ambient temperature and the resulting mixture was stirred at the

same temperature for three hours and a half. The solvent was evaporated under reduced pressure and the residue was dissolved in water and extracted with ether. The aqueous layer was separated, acidified to pH 2 with concentrated hydrochloric acid and extracted with ethyl acetate. The organic extract was washed with brine, dried over magnesium sulfate, filtered and concentrated in vacuo. The residue was triturated with 50% ether/hexane (v/v) to give (2S)-2-tert-butoxycarbonylamino-3-(3,4-dimethoxyphenyl)propanoic acid (5.35 g) as a white amorphous solid.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.42 (3x3H, s), 3.04 (1H, dd, J=14 and 6Hz), 3.13 (1H, dd, J=14 and 5.5Hz), 3.855 (3H, s), 3.862 (3H, s), 4.56 (1H, m), 4.92 (1H, br-d, J=7.5 Hz), 6.71 (1H, s), 6.72 (1H, d, J=8Hz), 6.80 (1H, d, J=8Hz);
MASS (ES+) m/e 324.

Preparation 121

To a stirred solution of tert-butyl (2R)-1-[(2S)-2-benzyloxycarbonylamino]-3-phenylpropanoylpyrrolidine-2-carboxylate (4.33 g) in methanol (40 ml) was added palladium on charchol (10%, 400 mg) and the mixture was stirred under 3 atm hydrogen atmosphere for eighteen hours. The reaction mixture was filtered through a Celite® pad. The filtrate was evaporated to give crude (1S)-1-benzyl-2-[(2R)-2-tert-butoxycarbonylpyrrolidin-1-yl]-2-oxoethylcarbamic acid (3.26 g) as an amorphous solid, which was used directly for the next step without further purification.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.30-2.20 (4H, m), 1.42 (9x4/5H, s), 1.48 (9x1/5H, s), 3.14 (1H, m), 3.37-3.77 (3H, m), 4.17 (1x4/5H, t, J=5Hz), 4.41 (1x1/5H, br), 4.64 (1x4/5H, m), 4.89 (1x1/5H, m), 7.12-7.45 (5H, m), 8.39 (2x1/5H, br), 8.63 (2x4/5H, br);
MASS (ES+) m/e 319.

Preparation 122

Compound (122) was obtained in a manner similar to Preparation 1.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.82-1.88 (13H, m), 1.45 (3x3H, s), 4.34 (1H, dt, J=8.5 and 5Hz), 4.86 (1H, d, J=8,5Hz);
MASS (ES-) m/e 270.

Preparation 123

Compound (123) was obtained in a manner similar to

Preparation 1.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.38 (3x3H, s), 5.10 (1H, d, J=8Hz), 7.25-7.43 (5H, m), 7.59 (1H, d, J=8Hz);

MASS (ES-) m/e 250.

Preparation 124

Compound (124) was obtained in a manner similar to Preparation 1.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.96 (3H, d, J=7.0 Hz), 0.99 (3H, d, J=7.0Hz), 1.41-1.49 (1H, m), 1.45 (9H, s), 1.47 (3H, s), 2.28 (1H, brs), 5.04 (1H, brs);

MASS (ES+) m/e 232.10 (M+1).

Preparation 125

Compound (125) was obtained in a manner similar to Preparation 1.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.42 (9H, s), 3.21 (1H, s), 3.27 (1H, s), 3.66 (1H, s), 3.72 (1H, s), 5.13 (1H, brs), 7.16-7.28 (4H, m);

MASS (ES-) m/e 276.12 (M-1).

Preparation 126

Compound (126) was obtained in a manner similar to Preparation 1.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 4.84-5.12 (1H, br), 2.19-2.34 (2H, m), 1.70-2.04 (6H, m), 1.44 (9H, s), 1.28-1.49 (1H, m);

MASS (ES+) m/e 230.14 (M+1).

Preparation 127

Compound (127) was obtained in a manner similar to Preparation 15.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.87 (3H, d, J=7.0Hz), 0.91 (3H, d, J=7.0Hz), 1.36-1.54 (1H, m), 1.41 (9H, s), 1.43 (3H, s), 1.72-1.96 (3H, m), 2.10-2.35 (1H, m), 2.58-2.68 (1H, m), 2.93 (1H, dd, J=12.8 and 9.5Hz), 3.11 (1H, dd, J=12.8 and 5.1Hz), 3.47-3.59 (1H, m), 4.35 (1H, dd, J=8.1 and 4.0Hz), 4.65-4.99 (2H, m), 5.06-5.22 (2H, m), 7.04-7.39 (11H, m);

MASS (ES+) m/e 566.30 (M+1).

Preparation 128

Compound (128) was obtained in a manner similar to Preparation 16.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.81 (3H, d, J=6.9Hz), 0.92 (3H, d, J=6.6Hz), 1.08-1.99 (11H, m), 1.43 (9H, s), 1.46 (3H, s), 2.22-

2.39 (1H, m), 2.72-2.90 (1H, m), 2.95-3.09 (1H, m), 3.52-3.61 (1H, m), 3.93-4.09 (1H, m), 4.30-4.39 (1H, m), 4.31 (2H, t, J=6.6Hz), 4.69-4.76 (1H, m), 4.95 (1H, dt, J=8.4 and 5.9Hz), 5.10-5.23 (2H, m), 6.78 (1H, s), 7.05-7.37 (11H, m), 7.39-7.48 (2H, m), 7.51-7.61 (1H, m), 8.00-8.07 (2H, m);
MASS (ES+) m/e 799.41 (M+1).

Preparation 129

Compound (129) was obtained in a manner similar to Preparation 18.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.55-0.70 (3H, m), 0.80-1.04 (3H, m), 1.29 (3H, s), 1.54-2.22 (12H, m), 2.46-2.62 (1H, m), 2.85-3.09 (2H, m), 3.73-3.88 (1H, m), 4.00-4.39 (3H, m), 4.91-5.04 (1H, m), 7.14-7.31 (6H, m), 7.35-7.45 (2H, m), 7.47-7.57 (1H, m), 7.85 (1H, br), 7.95-8.05 (2H, m), 8.24 (2H, br);
MASS (ES+) m/e 609.3 (Free, M+1).

Preparation 130

Compound (130) was obtained in a manner similar to Preparation 76.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.70 (3H, d, J=7.0Hz), 0.85 (3H, d, J=6.6Hz), 1.14 (3H, s), 1.32-2.00 (9H, m), 2.10-2.40 (2H, m), 2.99 (1H, dd, J=13.9 and 7.0Hz), 3.20 (1H, dd, J=13.9 and 8.8Hz), 3.26-3.37 (1H, m), 3.82-3.92 (1H, m), 4.18-4.29 (1H, m), 4.31 (2H, t, J=6.6Hz), 4.65-4.71 (1H, m), 5.15-5.26 (1H, m), 5.75 (1H, s), 7.12 (1H, d, J=10.6Hz), 7.15-7.31 (5H, m), 7.39-7.47 (2H, m), 7.52-7.62 (2H, m), 7.99-8.06 (2H, m);
MASS (ES+) m/e 591.37 (M+1).

Preparation 131

Compound (131) was obtained in a manner similar to Preparation 77.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.70 (3H, d, J=7.0Hz), 0.88 (3H, d, J=6.6Hz), 1.15 (3H, s), 1.22-1.94 (9H, m), 2.09-2.37 (2H, m), 2.99 (1H, dd, J=13.9 and 7.0Hz), 3.20 (1H, dd, J=13.9 and 8.8Hz), 3.26-3.37 (2H, m), 3.65 (2H, t, J=6.2Hz), 3.82-3.93 (1H, m), 4.17-4.28 (1H, m), 4.65-4.72 (1H, m), 5.15-5.26 (1H, m), 5.85 (1H, s), 7.12 (1H, d, J=10.3Hz), 7.16-7.31 (5H, m), 7.58 (1H, d, J=10.3Hz);
MASS (ES+) m/e 487.39 (M+1).

Preparation 132

Compound (132) was obtained in a manner similar to

Preparation 78. The obtained compound was used in Example 62. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.71 (3H, d, J=7.0Hz), 0.89 (3H, d, J=6.6Hz), 1.15 (3H, s), 1.48-1.94 (6H, m), 2.09-2.41 (2H, m), 2.43-2.55 (2H, m), 2.99 (1H, dd, J=13.6 and 7.0Hz), 3.20 (1H, dd, J=13.6 and 8.8Hz), 3.25-3.37 (2H, m), 3.89 (1H, dt, J=8.4 and 4.8Hz), 4.24 (1H, ddd, J=10.3, 7.3 and 7.0Hz), 4.66-4.72 (1H, m), 5.21 (1H, m), 7.53 (1H, d, J=10.3Hz), 9.77 (1H, dd, J=1.1 and 1.5Hz);

MASS (ES+) m/e 485.40 (M+1).

Preparation 133

Compound (133) was obtained in a manner similar to Preparation 15.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.35 (9H, s), 1.71-1.95 (3H, m), 2.52-2.61 (1H, m), 2.69 (1H, dd, J=12.8 and 9.5Hz), 2.90 (1H, dd, J=12.8 and 5.1Hz), 3.02-3.20 (2H, m), 3.23-3.33 (1H, m), 3.43-3.61 (1H, m), 4.31 (1H, dd, J=8.4 and 4.3Hz), 4.41-4.53 (1H, m), 4.90 (1H, dt, J=9.5 and 5.1Hz), 4.95-5.05 (1H, m), 5.08 (1H, d, J=12.5Hz), 5.17 (1H, d, J=12.5Hz), 6.68 (1H, d, J=7.3Hz), 6.96-7.48 (13H, m), 7.63 (1H, s), 7,74-7.82 (3H, m);

MASS (ES+) m/e 650.50 (M+1).

Preparation 134

Compound (134) was obtained in a manner similar to Preparation 16.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.13-1.29 (2H, m), 1.30-1.98 (8H, m), 1.39 (9H, s), 2.58-2.70 (1H, m), 2.71-3.00 (2H, m), 3.08-3.20 (1H, m), 3.21-3.35 (1H, m), 3.47-3.59 (1H, m), 3.97-4.17 (3H, m), 4.27-4.35 (1H, m), 4.79-4.95 (2H, m), 5.03-5.18 (1H, m), 5.09 (1H, d, J=12.5Hz), 5.16 (1H, d, J=12.5Hz), 6.74-6.92 (1H, m), 7.07-7.46 (16H, m), 7.50-7.59 (1H, m), 7.61 (1H, s), 7.72-7.79 (3H, m), 8.01 (2H, d, J=7.7Hz):

MASS (ES+) m/e 883.63 (M+1).

Preparation 135

Compound (135) was obtained in a manner similar to Preparation 17.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.09-2.11 (10H, m), 1.38 (9H, s), 2.60-2.73 (1H, m), 2.72-2.82 (1H, m), 2.83-2.96 (1H, m), 3.10-3.21 (1H, m), 3.24-3.39 (1H, m), 3.59-3.76 (1H, m), 3.99-4.14 (3H, m), 4.20-4.36 (1H, m), 4.71-4.95 (2H, m), 5.26-5.36 (1H, m), 7.05-7.15 (1H, m), 7.16-7.26 (5H, m), 7.27-7.34 (1H, m), 7.35-

7.47 (4H, m), 7.50-7.64 (3H, m), 7.70-7.80 (3H, m), 7.97-8.06 (2H, m);
MASS (ES+) m/e 793.47 (M+1).

Preparation 136

Compound (136) was obtained in a manner similar to Preparation 18.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.83-1.91 (10H, m), 2.45-3.11 (4H, m), 3.14-3.32 (1H, m), 3.55-3.69 (1H, m), 3.75-3.94 (2H, m), 4.04-4.14 (1H, m), 4.18-4.34 (1H, m), 4.47-4.64 (1H, m), 5.11-5.25 (1H, m), 7.03-7.55 (14H, m), 7.62-7.81 (3H, m), 7.85-8.15 (4H, m), 8.38 (1H, br);
MASS (ES+) m/e 693.47 (free, M+1).

Preparation 137

Compound (137) was obtained in a manner similar to Preparation 76.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.18-1.53 (2H, m), 1.59-1.94 (3H, m), 2.06-2.40 (5H, m), 2.86 (1H, dd, J=13.2 and 5.1Hz), 3.01 (1H, dd, J=13.9 and 7.0Hz), 3.03-3.15 (1H, m), 3.18 (1H, dd, J=13.2 and 10.6Hz), 3.39 (1H, dd, J=13.9 and 8.4Hz), 3.90-4.00 (1H, m), 4.19-4.35 (1H, m), 4.25 (2H, t, J=6.6Hz), 4.59-4.65 (1H, m), 4.81-4.91 (1H, m), 5.07 (1H, dt, J=10.6 and 5.1Hz), 6.33 (1H, d, J=9.9Hz), 6.47 (1H, d, J=10.6Hz), 7.13-7.29 (5H, m), 7.34 (1H, dd, J=8.4 and 1.5Hz), 7.37-7.49 (5H, m), 7.52-7.59 (1H, m), 7.67 (1H, s), 7.73-7.83 (3H, m), 7.99-8.05 (2H, m);
MASS (ES+) m/e 675.50 (M+1).

Preparation 138

Compound (138) was obtained in a manner similar to Preparation 77.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.20-1.89 (9H, m), 2.14-2.39 (2H, m), 2.85 (1H, dd, J=13.6 and 5.1Hz), 3.00 (1H, dd, J=14.3 and 6.6Hz), 3.04-3.13 (1H, m), 3.17 (1H, dd, J=13.6 and 10.6Hz), 3.38 (1H, dd, J=14.3 and 8.4Hz), 3.57 (2H, t, J=6.2Hz), 3.90-3.99 (1H, m), 4.28 (1H, dt, J=10.3 and 7.7Hz), 4.58-4.65 (1H, m), 4.80-4.90 (1H, m), 5.06 (1H, dt, J=10.6 and 5.1Hz), 6.39 (1H, d, J=9.9Hz), 6.48 (1H, d, J=10.6Hz), 7.12-7.28 (6H, m), 7.34 (1H, dd, J=10.3 and 1.8Hz), 7.41-7.50 (2H, m), 7.67 (1H, m), 7.73-7.83 (3H, m);
MASS (ES+) m/e 571.35 (M+1).

Preparation 139

Compound (139) was obtained in a manner similar to

Preparation 78.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.45-1.88 (6H, m), 2.13-2,48 (4H, m), 2.86 (1H, dd, J=13.6 and 5.1Hz), 3.02 (1H, dd, J=14.3 and 7.0Hz), 3.06-3.16 (1H, m), 3.18 (1H, dd, J=13.6 and 10.6Hz), 3.40 (1H, dd, J=14.3 and 8.4Hz), 3.91-4.01 (1H, m), 4.29 (1H, dt, J=10.3 and 7.0Hz), 4.58-4.67 (1H, m), 4.80-4.92 (1H, m), 5.07 (1H, dt, J=10.6 and 5.1Hz), 6.33 (1H, d, J=9.9Hz), 6.44 (1H, d, J=10.3Hz), 7.13-7.29 (6H, m), 7.35 (1H, dd, J=8.4 and 1.5Hz), 7.40-7.52 (2H m), 7.67 (1H, s), 7.74-7.85 (3H, m), 9.69 (1H, s);

MASS (ES+) m/e 569.35 (M+1).

Preparation 140

Compound (140) was obtained in a manner similar to Preparation 15.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.36-1.54 (1H, m), 1.43 (9H, s), 1.71-1.98 (3H, m), 2.55-2.66 (1H, m), 2.86-3.11 (3H, m), 3.44-3.62 (1H, m), 3.45 (2H, d, J=16.6Hz), 3.76 (2H, d, J=16.6Hz), 4.34-4.40 (1H, m), 4.98 (1H, ddd, J=9.5, 8.8 and 5.1Hz), 5.04-5.14 (1H, m), 5.10 (1H, d, J=12.5Hz), 5.19 (1H, d, J=12.5Hz), 7.07 (1H, d, J=8.8Hz), 7.12-7.30 (8H, m), 7.30-7.40 (5H, m);

MASS (ES+) m/e 612.49 (M+1).

Preparation 141

Compound (141) was obtained in a manner similar to Preparation 16.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.37 (6H, s), 1.43 (3H, s), 1.48-2.03 (10H, m), 2.66-2.78 (1H, m), 2.84-3.05 (2H, m), 3.13-3.26 (1H, m), 3.27-3.49 (2H, m), 3.53-3.67 (2H, m), 3.92-4.06 (1H, m), 4.17-4.38 (3H, m), 4.88-5.00 (1H, m), 5.07-5.27 (3H, m), 6.86-6.97 (1H, m), 7.09-7,37 (15H, m), 7.38-7.47 (2H, m), 7.51-7.59 (1H, m), 7.98-8.06 (2H, m);

MASS (ES+) m/e 845.56 (M+1).

Preparation 142

Compound (142) was obtained in a manner similar to Preparation 17.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.38 (6H, s), 1.45 (3H, s), 1.50-1.89 (8H, m), 1.88-2.19 (1H, m), 2.65-2.79 (1H, m), 2.95-3.34 (4H, m), 3.45-3.76 (4H, m), 3.92-4.05 (1H, m), 4.17-4.39 (4H, m), 4.78-4.92 (1H, m), 5.13-5.35 (1H, m), 7.00-7.32 (10H, m), 7.39-7.60 (4H, m), 7.98-8.07 (2H, m);

MASS (ES+) m/e 755.32 (M+1).

Preparation 143

Compound (143) was obtained in a manner similar to Preparation 18.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.17-1.46 (2H, m), 1.53-2.16 (8H, m), 2.86-3.14 (2H, m), 3.26-3.78 (6H, m), 4.03-4.32 (4H, m), 4.89-5.01 (1H, m), 7.00-7.31 (9H, m), 7.33-7.43 (2H, m), 7.47-7.55 (1H, m), 7.73 (1H, brs), 7.94-8.14 (4H, m), 8.30 (1H, brs), 8.86 (1H, brs);

MASS (ES+) m/e 655.37 (free, M+1).

Preparation 144

Compound (144) was obtained in a manner similar to Preparation 76.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.30-1.58 (4H, m), 1.66-1.94 (6H, m), 2.10-2.39 (2H, m), 2.93 (1H, dd, J=13.2 and 5.1Hz), 3.09-3.21 (1H, m), 3.30 (1H, dd, J=13.2 and 10.3Hz), 3.61 (1H, d, J=16.5Hz), 3.89-4.01 (1H, m), 3.94 (2H, d, J=16.5Hz), 4.17-4.38 (3H, m), 4.63-4.69 (1H, m), 5.14 (1H, dt, J=10.3 and 5.1Hz), 6.31 (1H, s), 7.05-7.31 (9H, m), 7.37-7.57 (4H, m), 7,99-8.04 (2H, m);

MASS (ES+) m/e 637.30 (M+1).

Preparation 145

Compound (145) was obtained in a manner similar to Preparation 77.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.21-1.89 (9H, m), 2.08-2.39 (2H, m), 2.85 (1H, d, J=16.8Hz), 2.93 (1H, dd, J=13.2 and 5.1Hz), 3.10-3.21 (1H, m), 3.30 (1H, dd, J=13.2, 10.3Hz). 3.62 (1H, d, J=16.8Hz), 3.63 (2H, t, J=6.2Hz), 3.89-4.00 (1H, m), 3.97 (2H, d, J=16.8Hz), 4.22 (1H, dt, J=10.3 and 7.7Hz), 4.64-4.70 (1H, m), 5.14 (1H, dt, J=10.3 and 5.1Hz), 6.51 (1H, s), 7.12-7.30 (10H, m), 7.52 (1H, d, J=10.3Hz);

MASS (ES+) m/e 533.34 (M+1).

Preparation 146

Compound (146) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 68.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.46-1.87 (6H, m), 2.07-2.44 (2H, m), 2.46 (2H, dt, J=7.0 and 1.5Hz), 2.86 (1H, d, J=16.2Hz), 2.92 (1H, dd, J=13.2 and 5.1Hz), 3.08-3.20 (1H, m), 3.29 (1H, dd, J=13.2 and 10.6Hz), 3.61 (1H, d, J=16.2Hz), 3.87-4.00 (1H, m), 3.96 (2H, d, J=16.2Hz), 4.23 (1H, ddd, J=10.3, 7.7 and 7.0Hz), 4.62-4.71 (1H, m), 5.14 (1H, dt, J=10.6 and 5.1Hz), 6.44 (1H, s), 7.13-7.31

(10H, m), 7.48 (1H, d, J=10.3Hz), 9.73 (1H, t, J=1.5Hz);
MASS (ES+) m/e 531.28 (M+1).

Preparation 147

Compound (147) was obtained in a manner similar to Preparation 14.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.18-1.51 (2H, m), 1.42 (9H, s), 1.57-1.83 (2H, m), 2.48-2.58 (1H, m), 3.11 (1H, dd, J=12.8 and 9.5Hz), 3.23 (1H, dd, J=12.8 and 5.3Hz), 3.41-3.52 (1H, m), 4.31-4.39 (1H, m), 4.72 (1H, dt, J=9.5 and 5.3Hz), 5.09 (1H, d, J=12.5Hz), 5.19 (1H, d, J=12.5Hz), 5.43 (1H, d, J=8.8Hz), 7.26-7.39 (5H, m), 7.39-7.49 (2H, m), 7.66 (1H, s), 7.69-7.81 (4H, m);
MASS (ES+) m/e 503.38 (M+1).

Preparation 148

Compound (148) was obtained in a manner similar to Preparation 15.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.80 (3H, t, J=7.3Hz), 1.20-2.06 (3H, m), 1.36 (3H, s), 1.41 (2H, s), 1.44 (7H, s), 2.55-2.66 (1H, m), 3.12 (1H, dd, J=12.8 and 9.2Hz), 3.18-3.28 (1H, m), 3.23 (1H, dd, J=12.8 and 5.1Hz), 3.45-3.62 (2H, m), 4.33-4.39 (1H, m), 4.97-5.16 (2H, m), 5.09 (1H, d, J=12.5Hz), 5.15 (1H, d, J=12.5Hz), 6.90 (1H, d, J=8.4Hz), 7.28-7.49 (8H, m), 7.67 (1H, s), 7.70-7.81 (4H, m);
MASS (ES+) m/e 602.46 (M+1).

Preparation 149

Compound (149) was obtained in a manner similar to Preparation 16.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.72 (3H, t, J=7.3Hz), 1.31-2.07 (11H, m), 1.43 (9H, s), 1.48 (3H, s), 2.13-2.32 (1H, m), 2.68-2.78 (1H, m), 3.17 (2H, d, J=7.3Hz), 3.52-3.63 (1H, m), 4.00-4.12 (1H, m), 4.31 (2H, t, J=6.2Hz), 4.35-4.40 (1H, m), 4.92-5.23 (4H, m), 6.73-6.92 (1H, m), 6.97 (1H, s), 7.24-7.49 (12H, m), 7.51-7.82 (3H, m), 8.00-8.06 (2H, m);
MASS (ES+) m/e 835.60 (M+1).

Preparation 150

Compound (150) was obtained in a manner similar to Preparation 17.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.76 (3H, t, J=7.0Hz), 1.43 (9H, s), 1.58-1.98 (15H, m), 2.65-2.78 (1H, m), 3.04-3.28 (2H, m), 3.65-3.77 (1H, m), 4.05-4.15 (1H, m), 4.22-4.38 (3H, m), 4.93-5.05 (1H,

m), 5.50-5.60 (1H, m), 6.81 (1H, s), 7.22-7.58 (7H, m), 7.65 (1H, s), 7.68-7.83 (3H, m), 7.98-8.05 (2H, m);
MASS (ES+) m/e 745.52 (M+1).

Preparation 151

Compound (151) was obtained in a manner similar to Preparation 18.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.59-0.74 (3H, m), 1.07-2.19 (13H, m), 1.37 (3H, s), 2.91-3.31 (3H, m), 3.65-3.78 (1H, m), 4.06-4.38 (4H, m), 4.99-5.10 (1H, m), 7.21-7.54 (7H, m), 7.60-7.78 (4H, m), 7.94-8.02 (2H, m), 8.08-8.49 (3H, m);
MASS (ES+) m/e 645.57 (free, M+1).

Preparation 152

Compound (152) was obtained in a manner similar to Preparation 76.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.81 (3H, t, J=7.0Hz), 1.28 (3H, s), 1.36-1.56 (2H, m), 1.62-1.99 (6H, m), 2.07-2.22 (2H, m), 2.22-2.41 (2H, m), 3.12 (1H, dd, J=13.6 and 5.9Hz), 3.18-3.30 (1H, m), 3.41 (1H, dd, J=13.6 and 9.9Hz), 3.81-3.92 (1H, m), 4,19-4.31 (1H, m), 4.32 (2H, t, J=6.2Hz), 4.61-4.68 (1H, m), 5.30 (1H, dt, J=9.9 and 5.9Hz), 5.91 (1H, s), 7.16 (1H, d, J=10.6Hz), 7.35-7.49 (5H, m), 7.51-7.59 (1H, m), 7.64 (1H, d, J=9.9Hz), 7.69 (1H, s), 7.73-7.83 (3H, m), 8.00-8.06 (2H, m);
MASS (ES+) m/e 627.44 (M+1).

Preparation 153

Compound (153) was obtained in a manner similar to Preparation 77.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (3H, t, J=7.3Hz), 1.28-1.52 (2H, m), 1.29 (3H, s), 1.53-1.96 (7H, m), 2.08-2.25 (2H, m), 2.25-2.41 (2H, m), 3.13 (1H, dd, J=13.6 and 5.9Hz), 3.19-3.30 (1H, m), 3,42 (1H, dd, J=13.6 and 9.9Hz), 3.67 (2H, t, J=6.6Hz), 3.82-3.92 (1H, m), 4.24 (1H, dt, J=10.3 and 7.3Hz), 4.61-4.68 (1H, m), 5.30 (1H, dt, J=9.9 and 5.9Hz), 5.95 (1H, s), 7.15 (1H, d, J=10.3Hz), 7.35-7.50 (3H, m), 7.63 (1H, d, J=10.3Hz), 7.69 (1H, s), 7.72-7.83 (3H, m);
MASS (ES+) m/e 523.38 (M+1).

Preparation 154

Compound (154) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 71.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.83 (3H, t, J=7.3Hz), 1.29 (3H, s),

1.49-1.93 (6H, m), 2.08-2.23 (2H, m), 2.24-2.39 (2H, m), 2.45-2.55 (2H, m), 3.12 (1H, dd, J=13.6 and 5.9Hz), 3.18-3.29 (1H, m), 3.41 (1H, dd, J=13.6 and 9.9Hz), 3.82-3.93 (1H, m), 4.18-4.30 (1H, m), 4.61-4.68 (1H, m), 5.30 (1H, dt, J=9.9 and 5.9Hz), 5.87 (1H, s), 7.15 (1H, d, J=10.3Hz), 7.37 (1H, dd, J=8.4 and 1.8Hz), 7.42-7.49 (2H, m), 7.57 (1H, d, J=10.3Hz), 7.69 (1H, s), 7.74-7.83 (3H, m), 9.77 (1H, s);
MASS (ES+) m/e 521.33 (M+1).

Preparation 155

Compound (155) was obtained in a manner similar to Preparation 15.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.40 (9H, s), 1.40-1.50 (1H, m), 1.71-1.96 (3H, m), 2.50-2.85 (3H, m), 2.95-3.28 (2H, m), 3.45-3.60 (1H, m), 3.72 (3H, s), 4.30 (1H, dd, J=7.3 and 4.1Hz), 4.39-4.51 (1H, m), 4.81-4.92 (1H, m), 5.00-5.20 (1H, m), 5.07 (1H, d, J=12.1Hz), 5.14 (1H, d, J=12.1Hz), 6.58 (1H, d, J=8.1Hz), 6.88 (1H, s), 7.08-7.37 (13H, m), 7.63 (1H, d, J=8.1Hz);
MASS (ES+) m/e 653.51 (M+1).

Preparation 156

Compound (156) was obtained in a manner similar to Preparation 16.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.26-1.97 (14H, m), 1.39 (9H, s), 2.53-2.78 (2H, m), 2.94-3.31 (2H, m), 3.49-3.62 (1H, m), 3.71 (3H, s), 3.94-4.05 (1H, m), 4.16-4.36 (2H, m), 4.67-4.84 (1H, m), 4.99-5.19 (1H, m), 5.06 (1H, d, J=12.5Hz), 5.13 (1H, d, J=12.5Hz), 6.62-6.77 (1H, m), 6.86 (1H, s), 7.01-7.46 (15H, m), 7.50-7.57 (1H, m), 7.64 (1H, d, J=7.7Hz), 7.99-8.06 (2H, m);
MASS (ES+) m/e 886.62 (M+1).

Preparation 157

Compound (157) was obtained in a manner similar to Preparation 17.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.16-2.14 (12H, m), 1.38 (9H, s), 2.49-2.67 (2H, m), 2.73-2.85 (1H, m), 3.08-3.28 (2H, m), 3.53-3.72 (1H, m), 3.72 (3H, s), 3.86-3.97 (1H, m), 4.18-4.35 (3H, m), 4.43-4.59 (1H, m), 4.60-4.74 (1H, m), 5.46 (1H, brs), 6.91 (1H, s), 7.00-7.12 (3H, m), 7.15-7.32 (5H, m), 7.38-7.47 (2H, m), 7.51-7.61 (2H, m); 7.99-8.06 (2H, m);
MASS (ES+) m/e 796.59 (M+1).

Preparation 158

Compound (158) was obtained in a manner similar to Preparation 18.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.03-1.20 (2H, m), 1.36-1.96 (11H, m), 2.63-3.23 (6H, m), 3.65 (3H, s), 3.97-4.20 (3H, m), 4.41-4.55 (1H, m), 4.96-5.13 (1H, m), 7.01-7.31 (9H, m), 7.36-7.45 (2H, m), 7.46-7.57 (1H, m), 7.62-7.70 (1H, m), 7.88-8.24 (4H, m);
MASS (ES+) m/e 696.53 (free, M+1).

Preparation 159

Compound (159) was obtained in a manner similar to Preparation 76.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.34-1.53 (2H, m), 1.63-1.95 (6H, m), 2.13-2.38 (2H, m), 2.86 (1H, dd, J=13.2 and 5.5Hz), 3.00 (1H, dd, J=14.2 and 6.6Hz), 3.04-3.22 (1H, m), 3.17 (1H, dd, J=13.2 and 9.9Hz), 3.35 (1H, dd, J=14.2 and 11.0Hz), 3.70 (3H, s), 3.87-4.06 (1H, m), 4.28 (2H, t, J=6.6Hz), 4.29-4.37 (1H, m), 4.59-4.65 (1H, m), 4.78-4.88 (1H, m), 5.08 (1H, dt, J=11.0 and 5.5Hz), 6.42 (1H, d, J=9.9Hz), 6.54 (1H, d, J=11.0Hz), 6.87 (1H, s), 7.08-7.31 (9H, m), 7.40-7.49 (2H, m), 7.55 (1H, d, J=7.7Hz), 7.59 (1H, d, J=7.7Hz), 8.00-8.07 (2H, m);
MASS (ES+) m/e 678.40 (M+1).

Preparation 160

Compound (160) was obtained in a manner similar to Preparation 77.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.21-1.92 (9H, m), 2.10-2.39 (2H, m), 2.86 (1H, dd, J=14.7 and 6.6Hz), 2.99 (1H, dd, J=13.6 and 5.5Hz), 3.04-3.15 (1H, m), 3.17 (1H, dd, J=13.6 and 10.6Hz), 3.34 (1H, dd, J=14.7 and 9.2Hz), 3.62 (2H, t, J=6.2Hz), 3.72 (3H, s), 3.91-4.01 (1H, m), 4.29 (1H, dt, J=10.3 and 7.7Hz), 4.59-4.65 (1H, m), 4.81 (1H, dt, J=9.2 and 6.6Hz), 5.08 (1H, dt, J=10.6 and 5.5Hz), 6.44 (1H, d, J=10.3Hz), 6.48 (1H, d, J=10.6Hz), 6.87 (1H, s), 7.08-7.31 (9H, m), 7.60 (1H, dd, J=8.1 and 0.7Hz);
MASS (ES+) m/e 574.42 (M+1).

Preparation 161

Compound (161) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 74.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.40-1.91 (5H, m), 2.14-2.40 (2H, m), 2.44 (2H, dt, J=6.6 and 1.5Hz), 2.86 (1H, dd, J=13.2 and 10.6Hz), 2.99 (1H, dd, J=14.7 and 6.2Hz), 3.04-3.15 (1H, m), 3.17 (1H, dd, J=13.2 and 10.6Hz), 3.34 (1H, dd, J=14.7 and 8.4Hz), 3.73 (3H, s),

3.92-4.01 (1H, m), 4.29 (1H, dt, J=10.3 and 7.3Hz), 4.58-4.65 (1H, m), 4.81 (1H, dt, J=9.9 and 6.2Hz), 5.08 (1H, dt, J=10.6 and 5.1Hz), 6.33 (1H, d, J=10.3Hz), 6.43 (1H, d, J=10.3Hz), 6.87 (1H, s), 7.07-7.36 (9H, m), 7.60 (1H, s, J=7.7Hz), 9.73 (1H, s);
MASS (ES+) m/e 572.35 (M+1).

Preparation 162

Compound (162) was obtained in a manner similar to Preparation 14.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.43 (9H, s), 1.45-1.61 (1H, m), 1.76-2.00 (3H, m), 2.29 (3H, s), 2.63-2.75 (1H, m), 2.84-3.06 (2H, m), 3.48-3.66 (1H, m), 4.32-4.39 (1H, m), 4.56-4.66 (1H, m), 5.07-5.23 (2H, m), 5.33-5.42 (1H, m), 7.02-7.12 (4H, m), 7.30-7.39 (5H, m);
MASS (ES+) m/e 467.38 (M+1).

Preparation 163

Compound (163) was obtained in a manner similar to Preparation 15.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.80 (3H, t, J=7.5Hz), 1.38 (3H, s), 1.41 (3H, s), 1.43 (6H, s), 1.45-1.64 (2H, m), 1.75-2.14 (4H, m), 2.30 (3H, s), 2.69-2.84 (1H, m), 2.91 (1H, dd, J=13.2 and 9.0Hz), 3.03 (1H, dd, J=13.2 and 5.7Hz), 3.50-3.61 (1H, m), 4.34-4.40 (1H, m), 4.93 (1H, dt, J=9.0 and 5.7Hz), 5.04-5.24 (3H, m), 6.88 (1H, d, J=9.0Hz), 6.93-7.13 (5H, m), 7.29-7.40 (5H, m);
MASS (ES+) m/e 566.52 (M+1).

Preparation 164

Compound (164) was obtained in a manner similar to Preparation 16.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.72 (3H, t, J=6.6Hz), 1.38-2.00 (13H, m), 1.44 (9H, s), 1.49 (3H, s), 2.30 (3H, s), 2.75-3.00 (2H, m), 3.53-3.64 (1H, m), 3.98-4.12 (1H, m), 4.32 (2H, t, J=6.6Hz), 4.39 (1H, dd, J=8.2 and 4.4Hz), 4.85-4.96 (1H, m), 5.06-5.19 (3H, m), 6.67-6.82 (1H, m), 6.91-7.01 (1H, m), 7.04-7.11 (4H, m), 7.29-7.37 (5H, m), 7.39-7.47 (2H, m), 7.51-7.60 (1H, m), 8.00-8.06 (2H, m);
MASS (ES+) m/e 799.47 (M+1).

Preparation 165

Compound (165) was obtained in a manner similar to Preparation 17.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.79 (3H, t, J=10.5Hz), 1.45 (12H, s),

1.46-1.96 (12H, m), 2.11-2.24 (1H, m), 2.32 (3H, s), 2.72-2.84 (1H, m), 2.89-3.07 (2H, m), 3.65-3.76 (1H, m), 4.00-4.12 (1H, m), 4.26-4.40 (3H, m), 4.83-4.94 (1H, m), 5.38 (1H, brs), 6.78 (1H, s), 7.07-7.12 (4H, m), 7.16-7.22 (1H, d, J=8.1Hz), 7.40-7.48 (2H, m), 7.52-7.60 (1H, m), 8.01-8.07 (2H, m);
MASS (ES+) m/e 709.38 (M+1).

Preparation 166

Compound (166) was obtained in a manner similar to Preparation 18.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.64-0.75 (3H, m), 1.37 (3H, s), 1.54-2.14 (12H, m), 2.27 (3H, s), 2.81-3.07 (4H, m), 3.67-3.80 (1H, m), 4.17-4.37 (4H, m), 4.85-4.96 (1H, m), 7.00-7.12 (4H, m), 7.36-7.44 (2H, m), 7.49-7.64 (2H, m), 7.97-8.04 (2H, m), 8.07-8.43 (3H, m);
MASS (ES+) m/e 609.40 (free, M+1).

Preparation 167

Compound (167) was obtained in a manner similar to Preparation 76.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.82 (3H, t, J=7.3Hz), 1.28 (3H, s), 1.36-1.57 (2H, m), 1.62-1.98 (5H, m), 2.06-2.40 (4H, m), 2.30 (3H, s), 2.92 (1H, dd, J=13.6 and 6.3Hz), 3.15-3.33 (2H, m), 3.82-3.91 (1H, m), 4.25 (1H, dt, J=10.5 and 7.7Hz), 4.32 (2H, t, J=6.3Hz), 4.64-4.70 (1H, m), 5.17 (1H, dt, J=10.5 and 6.3Hz), 5.85 (1H, s), 7.04-7.16 (5H, m), 7.15 (1H, d, J=10.5Hz), 7.40-7.48 (2H, m), 7.50-7.60 (2H, m), 8.01-8.06 (2H, m);
MASS (ES+): m/e 591.56 (M+1).

Preparation 168

Compound (168) was obtained in a manner similar to Preparation 77.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (3H, t, J=7.3Hz), 1.22-1.94 (9H, m), 1.28 (3H, s), 2.07-2.40 (4H, m), 2.30 (3H, s), 2.91 (1H, dd, J=13.2 and 6.2Hz), 3.20 (1H, dd, J=13.2 and 9.9Hz), 3.22-3.32 (1H, m), 3.66 (2H, t, J=6.3Hz), 3.81-3.91 (1H, m), 4.23 (1H, dt, J=10.3 and 7.7Hz), 4.63-4.70 (1H, m), 5.16 (1H, dt, J=10.3 and 6.2Hz), 5.93 (1H, s), 7.04-7.14 (4H, m), 7.14 (1H, d, J=9.9Hz), 7.53 (1H, d, J=10.3Hz);
MASS (ES+): m/e 487.46 (M+1).

Preparation 169

Compound (169) was obtained in a manner similar to

Preparation 78. The obtained compound was used in Example 77. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (3H, t, J=7.3Hz), 1.29 (3H, s), 1.49-1.91 (6H, m), 2.08-2.39 (4H, m), 2.30 (3H, s), 2.45-2.54 (2H, t, J=6.3Hz), 2.91 (1H, dd, J=13.6 and 5.9Hz), 3.20 (1H, dd, J=13.6 and 10.3Hz), 3.22-3.32 (1H, m), 3.81-3.91 (1H, m), 4.23 (1H, dt, J=10.6 and 7.0Hz), 4.64-4.70 (1H, m), 5.15 (1H, dt, J=10.3 and 5.9Hz), 5.87 (1H, s), 7.05-7.14 (4H, m), 7.15 (1H, d, J=10.6Hz), 7.48 (1H, d, J=10.3Hz), 9.77 (1H, s);
MASS (ES+): m/e 485.39 (M+1).

Preparation 170

Compound (170) was obtained in a manner similar to Preparation 14.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.32-1.38 (9H, m), 1.56-2.31 (3H, m), 3.01-3.23 (2H, m), 3.33-3.43 (1H, m), 3.57-3.80 (1H, m), 4.36-4.44 (1H, m), 4.84-4.96 (1H, m), 5.05-5.23 (3H, m), 5.35-5.43 (1H, m), 7.07-7.20 (2H, m), 7.27-7.40 (5H, m), 7.49-7.62 (1H, m), 8.46-8.56 (1H, m);
MASS (ES+): m/e 454.31 (M+1).

Preparation 171

Compound (171) was obtained in a manner similar to Preparation 15.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.763 (3H, t, J=6.3Hz), 1.33-1.53 (2H, m), 1.36-1.40 (3H, m), 1.42 (9H, s), 1.73-2.37 (4H, m), 3.03-3.30 (2H, m), 3.35-3.87 (2H, m), 4.40-4.45 (1H, m), 5.06-5.29 (4H, m), 7.09-7.17 (2H, m), 7.20-7.24 (1H, m), 7.29-7.42 (5H, m), 7.52-7.64 (1H, m), 8.44-8.52 (1H, m);
MASS (ES+): m/e 553.39 (M+1).

Preparation 172

Compound (172) was obtained in a manner similar to Preparation 16.
MASS (ES+): m/e 786.49 (M+1).

Preparation 173

Compound (172) (crude compound) was purified by flash column chromatography (Silica gel column, eluting with 80 to 100% ethyl acetate/hexane (v/v) then 5% methanol ethyl acetate (v/v)) to give Compound (173) (1.36 g) as an amorphous solid.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.62-0.75 (3H, m), 1.33-2.27 (12H, m), 1.43 (9H, s), 3.02-3.29 (3H, m), 3.41-3.86 (2H, m), 4.00-4.10 (1H, m), 4.27-4.34 (2H, m), 4.40-4.46 (1H, m), 5.10-5.25 (4H, m),

6.96-7.02 (1H, m), 7.05-7.19 (2H, m), 7.28-7.48 (9H, m), 7.50-7.77 (3H, m), 8.00-8.06 (2H, m), 8.44-8.52 (1H, m);
MASS (ES+): m/e 786.41 (M+1).

Preparation 174

Compound (174) was obtained in a manner similar to Preparation 17.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.61-0.73 (3H, m), 1.30-2.31 (16H, m), 1.43 (9H, s), 3.08-3.30 (3H, m), 3.35-3.58 (1H, m), 3.78-4.07 (2H, m), 4.23-4.46 (3H, m), 5.11-5.24 (1H, m), 6.90-7.04 (1H, m), 7.13-7.31 (2H, m), 7.37-7.73 (5H, m), 7.99-8.06 (2H, m), 8.45-8.52 (1H, m);
MASS (ES+): m/e 696.49 (M+1).

Preparation 175

Compound (175) was obtained in a manner similar to Preparation 18.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.55-2.45 (19H, m), 2.75-3.92 (6H, m), 4.15-4.41 (3H, m), 6.90-6.92 (1H, m), 7.08-7.31 (2H, m), 7.35-7.61 (5H, m), 7.88-8.42 (3H, m), 8.80-8.95 (2H, m);
MASS (ES+): m/e 596.14 (free, M+1).

Preparation 176

Compound (176) was obtained in a manner similar to Preparation 76.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.83 (3H, t, J=7.5Hz), 1.29 (3H, s), 1.33-1.97 (8H, m), 2.02-2.43 (4H, m), 3.12 (1H, dd, J=15.0 and 6.0Hz), 3.52 (1H, dd, J=15.0 and 9.0Hz), 3.75-3.85 (1H, m), 3.87-3.98 (1H, m), 4.20-4.31 (1H, m), 4.31 (2H, t, J=6.8Hz), 4.64-4.72 (1H, m), 5.58 (1H, dt, J=9.0 and 6.0Hz), 5.87 (1H, s), 7.05-7.30 (4H, m), 7.39-7.62 (4H, m), 8.02 (2H, d, J=7.5Hz), 8.45 (1H, d, J=4.5Hz);
MASS (ES+): m/e 578.45 (M+1).

Preparation 177

Compound (177) was obtained in a manner similar to Preparation 77.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (1H, t, J=7.2Hz), 1.21-1.97 (8H, m), 1.29 (3H, s), 2.07-2.45 (4H, m), 3.12 (1H, dd, J=15.3 and 6.0Hz), 3.52 (1H, dd, J=15.3 and 10.5Hz), 3.65 (2H, t, J=6.0Hz), 3.74-3.84 (1H, m), 3.87-3.98 (1H, m), 4.25 (1H, dt, J=9.9 and 7.8Hz), 4.68 (1H, dd, J=7.8 and 2.7Hz), 5.58 (1H, dt, J=10.5 and 5.7Hz), 5.94-6.03 (1H, m), 7.06-7.13 (1H, m), 7.14-7.24 (2H, m),

7.42-7.64 (2H, m), 8.07-8.13 (1H, m), 8.42-8.48 (1H, m);
MASS (ES+): m/e 474.43 (M+1).

<u>Preparation 178</u>

Compound (178) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 80.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.85 (3H, t, J=7.3Hz), 1.30 (3H, s), 1.49-2.03 (8H, m), 2.09-2.44 (4H, m), 2.44-2.53 (2H, m), 3.12 (1H, dd, J=15.0 and 5.4Hz), 3.53 (1H, dd, J=15.0 and 9.9Hz), 3.74-3.85 (1H, m), 3.88-3.99 (1H, m), 4.26 (1H, dt, J=10.5 and 7.5Hz), 4.69 (1H, dd, J=7.5 and 2.4Hz), 5.58 (1H, dt, J=9.9 and 5.4Hz), 5.94 (1H, m), 7.07-7.13 (1H, m), 7.15-7.25 (2H, m), 7.42-7.50 (1H, m), 7.57 (1H, dt, J=7.5 and 1.8Hz), 8.43-8.47 (1H, m), 9.77 (1H, t, J=1.5Hz);
MASS (ES+): m/e 472.44 (M+1).

<u>Preparation 179</u>

Compound (179) was obtained in a manner similar to Preparation 77.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (3H, t, J=7.3Hz), 1.24-1.93 (8H, m), 1.28 (3H, s), 2.06-2.24 (2H, m), 2.16 (3H, s), 2.24-2.41 (2H, m), 2.91 (1H, dd, J=13.6 and 5.9Hz), 3.20 (1H, dd, J=13.6 and 9.9Hz), 3.21-3.33 (1H, m), 3.65 (2H, t, J=6.6Hz), 3.79-3.90 (1H, m), 4.17-4.29 (1H, m), 4.67 (1H, br-d, J=6.0Hz), 5.15 (1H, dt, J=9.9 and 6.2Hz), 6.00 (1H, s), 7.12 (1H, d, J=9.9Hz), 7.18 (2H, d, J=8.4Hz), 7.40 (2H, d, J=8.4Hz), 7.55 (1H, d, J=10.3Hz);
MASS (ES+): m/e 530.42 (M+1).

<u>Preparation 180</u>

Compound (180) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 83.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (3H, t, J=7.3Hz), 1.22-1.33 (1H, m), 1.29 (3H, s), 1.47-1.92 (5H, m), 2.08-2.39 (4H, m), 2.16 (3H, s), 2.50 (2H, br.t, J=6.6Hz), 2.91 (1H, dd, J=13.6 and 5.9Hz), 3.18-3.33 (1H, m), 3.20 (1H, d, J=13.6 and 9.9Hz), 3.80-3.91 (1H, m), 4.16-4.30 (1H, m), 4.66 (1H, br-d, J=6.7Hz), 5.15 (1H, dt, J=10.1 and 5.9Hz), 5.90 (1H, s), 7.13 (1H, d, J=7.3Hz), 7.15 (1H, s), 7.18 (2H, d, J=8.4Hz), 7.40 (2H, d, J=8.4Hz), 7.49 (1H, d, J=10.6Hz);
MASS (ES+): m/e 528.32 (M+1).

<u>Preparation 181</u>

Compound (181) was obtained in a manner similar to Preparation 13.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.07-1.31 (2H, m), 1.35 (4.5H, br.s), 1.45 (4.5H, br.s), 1.50-1.75 (3H, m), 2.10-2.32 (1H, m), 2.74-3.05 (1H, m), 3.81-4.10 (1H, m), 4.75 (0.5H, br.s), 4.95 (0.5H, br.s), 5.05-5.25 (2H, m), 7.25-7.40 (5H, m);

MASS (ES+): m/e 320.29 (M+1).

<u>Preparation 182</u>

Compound (182) was obtained in a manner similar to Preparation 14.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.49-0.69 (1H, m), 1.05-1.29 (1H, m), 1.42 (9H, s), 1.30-1.77 (3H, m), 2.14-2.25 (1H, m), 2.89-3.19 (3H, m), 3.48-3.62 (1H, m), 4.84-5.01 (1H, m), 5.08-5.23 (2H, m), 5.25-5.33 (1H, m), 5.43 (1H, br-d, J=8.1Hz), 7.02-7.40 (10H, m);

MASS (ES+): m/e 467.41 (M+1).

<u>Preparation 183</u>

Compound (183) was obtained in a manner similar to Preparation 15.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.54-0.72 (1H, m), 0.78 (2.1H, t, J=7.3Hz), 0.99 (0.9H, m, J=7.3Hz), 1.07-1.25 (1H, m), 1.31-2.03 (5H, m), 1.40 (3H, s), 1.42 (9H, s), 2.15-2.26 (1H, m), 2.66-3.20 (3H, m), 3.51-3.60 (1H, m), 4.98-5.30 (3H, m), 6.87-6.96 (0.7H, m), 7.02-7.10 (0.3H, m), 7.13-7.40 (11H, m);

MASS (ES+): m/e 566.46 (M+1).

<u>Preparation 184</u>

Compound (184) was obtained in a manner similar to Preparation 16.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.60-0.85 (1H, m), 0.70 (3H, t, J=7.3Hz), 1.08-1.30 (2H, m), 1.33-2.00 (9H, m), 1.44 (12H, s), 2.18-2.41 (2H, m), 2.92-3.21 (3H, m), 3.56-3.68 (1H, m), 3.95-4.16 (1H, m), 4.32 (2H, t, J=6.6Hz), 5.00-5.31 (4H, m), 6.79 (1H, br-d, J=8.1Hz), 6.99-7.08 (1H, m), 7.14-7.39 (6H, m), 7.40-7.48 (2H, m), 7.51-7.62 (1H, m), 8.00-8.08 (2H, m);

MASS (ES+): m/e 799.47 (M+1).

<u>Preparation 185</u>

Compound (185) was obtained in a manner similar to Preparation 17.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.59-0.78 (1H, m), 0.76 (3H, t, J=7.3Hz), 1.17-2.07 (13H, m), 1.40 (3H, s), 1.43 (9H, s), 2.19-

2.30 (1H, m), 2.86-3.20 (3H, m), 3.62-3.77 (1H, m), 3.96-4.09 (1H, m), 4.25-4.39 (2H, m), 5.13-5.25 (2H, m), 5.43 (1H, br.s), 6.96 (1H, br.s), 7.11-7.35 (6H, m), 7.39-7.49 (2H, m), 7.52-7.62 (1H, m), 8.00-8.08 (2H, m);

MASS (ES+): m/e 709.48 (M+1).

Preparation 186

Compound (186) was obtained in a manner similar to Preparation 18.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.50-0.91 (4H, m), 1.03-2.23 (13H, m), 1.40 (3H, br.s), 2.82-3.34 (3H, m), 3.42-3.66 (1H, m), 3.70-4.10 (1H, m), 4.19-4.52 (2H, m), 4.60-4.86 (1H, m), 5.05-5.28 (1H, m), 7.07-7.32 (5H, m), 7.34-7.47 (2H, m), 7.48-7.59 (1H, m), 7.83-8.17 (2H, m);

MASS (ES+): m/e 609.44 (free, M+1).

Preparation 187

Compound (187) was obtained in a manner similar to Preparation 76.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.75 (3H, t, J=7.3Hz), 1.20-2.16 (13H, m), 2.19-2.31 (1H, m), 2.93 (1H, dt, J=13.4 and 2.6Hz), 3.04 (1H, dd, J=13.9 and 7.3Hz), 3.21 (1H, dd, J=13.9 and 8.1Hz), 3.94-4.05 (1H, m), 4.19-4.32 (1H, m), 4.31 (2H, t, J=6.2Hz), 5.00-5.07 (1H, m), 5.36 (1H, dt, J=10.3 and 7.7Hz), 6.05 (1H, s), 6.53 (1H, d, J=10.6Hz), 7.16-7.32 (5H, m), 7.39-7.48 (2H, m), 7.49-7.60 (2H, m), 7.98-8.06 (2H, m);

MASS (ES+): m/e 591.49 (M+1).

Preparation 188

Compound (188) was obtained in a manner similar to Preparation 77.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.78 (3H, t, J=7.3Hz), 1.18-2.34 (14H, m), 1.27 (3H, s), 2.93 (1H, dt, J=13.2 and 2.6Hz), 3.04 (1H, dd, J=13.9 and 7.3Hz), 3.21 (1H, dd, J=13.9, 7.7Hz), 3.59-3.71 (2H, m), 4.00 (1H, br-d, J=13.6Hz), 4.20-4.32 (1H, m), 5.04 (1H, br-d, J=6.2Hz), 5.36 (1H, dt, J=10.3 and 7.7Hz), 6.16 (1H, s), 6.54 (1H, d, J=10.3Hz), 7.15-7.32 (5H, m), 7.54 (1H, d, J=9.9Hz);

MASS (ES+): m/e 487.40 (M+1).

Preparation 189

Compound (189) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 86.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.78 (3H, t, J=7.3Hz), 1.18-1.37 (1H, m), 1.29 (3H, s), 1.45-2.31 (1H, m), 2.47-2.56 (2H, m), 2.94 (1H, dt, J=13.5 and 2.9Hz), 3.04 (1H, dd, J=13.9 and 7.3Hz), 3.21 (1H, dd, J=13.9 and 7.7Hz), 3.98 (1H, br-d, J=13.2Hz), 4.18-4.31 (1H, m), 5.04 (1H, br-d, J=6.2Hz), 5.36 (1H, dt, J=9.7 and 7.9Hz), 5.98 (1H, s), 6.50 (1H, d, J=10.6Hz), 7.15-7.32 (5H, m), 7.43 (1H, d, J=9.9Hz), 9.76-9.79 (1H, m);

MASS (ES+): m/e 485.33 (M+1).

Preparation 190

Compound (190) was obtained in a manner similar to Preparation 77.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.82 (3H, t, J=7.3Hz), 1.22-1.72 (6H, m), 1.28 (3H, s), 1.74-1.93 (2H, m), 2.08-2.41 (4H, m), 2.96 (1H, dd, J=13.9 and 6.6Hz), 2.99 (3H, s), 3.20 (1H, dd, J=13.9 and 9.2Hz), 3.25-3.37 (1H, m), 3.65 (2H, t, J=6.4Hz), 3.79-3.91 (1H, m), 4.24 (1H, dt, J=10.3 and 7.5Hz), 4.70 (1H, br-d, J=7.7Hz), 5.15 (1H, dt, J=9.7 and 6.4Hz), 6.07 (1H, s), 6.65 (1H, br.s), 7.10 (1H, d, J=9.3Hz), 7.13 (2H, d, J=8.4Hz), 7.22 (2H, d, J=8.4Hz), 7.61 (1H, d, J=10.3Hz);

MASS (ES+): m/e 566.40 (M+1).

Preparation 191

Compound (191) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 90.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.83 (3H, t, J=7.3Hz), 1.29 (3H, s), 1.51-1.91 (4H, m), 2.08-2.39 (6H, m), 2.50 (2H, br.t, J=7.3Hz), 2.91-2.99 (1H, m), 2.99 (3H, s), 3.20 (1H, dd, J=13.9 and 9.2Hz), 3.25-3.36 (1H, m), 3.80-3.91 (1H, m), 4.18-4.30 (1H, m), 4.69 (1H, br-d, J=7.3Hz), 5.09-5.21 (1H, m), 6.01 (1H, s), 6.59 (1H, s), 7.07-7.17 (3H, m), 7.22 (2H, d, J=8.4Hz), 7.55 (1H, d, J=10.3Hz);

MASS (ES+): m/e 564.41 (M+1).

Preparation 192

Compound (192) was obtained in a manner similar to Preparation 14.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.43 (9H, m), 1.46-1.59 (1H, m), 1.72-2.02 (3H, m), 2.69-2.84 (1H, m), 2.98 (1H, dd, J=13.0 and 8.8Hz), 3.10 (1H, dd, J=13.0 and 5.5Hz), 3.49-3.67 (1H, m), 4.38 (1H, dd, J=8.1 and 3.7Hz), 4.68 (1H, dt, J=8.8 and 5.5Hz), 4.99-5.24 (2H, m), 5.40 (1H, d, J=8.8Hz), 7.23-7.60 (14H, m);

MASS (ES+): m/e 529.38 (M+1).

Preparation 193

Compound (193) was obtained in a manner similar to Preparation 15.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.81 (3H, t, J=7.4Hz), 1.38 (1.5H, s), 1.41 (1.5H, s), 1.44 (9H, s), 1.70-2.09 (4H, m), 2.74-2.95 (1H, m), 2.99 (1H, dd, J=13.3 and 9.6Hz), 3.13 (1H, dd, J=13.3 and 5.1Hz), 3.51-3.66 (1H, m), 4.39 (1H, dd, J=7.6 and 3.3Hz), 4.93-5.04 (1H, m), 5.06-5.26 (2H, m), 6.90 (1H, d, J=7.6Hz), 7.27-7.59 (14H, m);

MASS (ES+): m/e 628.50.

Preparation 194

Compound (194) was obtained in a manner similar to Preparation 16.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.58 (0.6H, t, J=7.3Hz), 0.73 (2.4H, t, J=7.3Hz), 1.42 (3H, s), 1.44 (9H, s), 1.48-2.03 (9H, m), 2.83-2.96 (1H, m), 2.99-3.14 (2H, m), 3.54-3.66 (1H, m), 3.93-4.15 (1H, m), 4.25-4.36 (2H, m), 4.40 (1H, dd, J=7.6 and 3.3Hz), 4.92-5.03 (1H, m), 5.06-5.21 (2H, m), 6.72-6.90 (1H, m), 6.98 (1H, s), 7.23-7.60 (19H, m), 7.99-8.06 (2H, m);

MASS (ES+): m/e 861.60 (M+1).

Preparation 195

Compound (195) was obtained in a manner similar to Preparation 17.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.77 (3H, t, J=7.3Hz), 1.44 (12H, s), 1.46-2.21 (12H, m), 2.81-2.94 (1H, m), 3.00-3.11 (2H, m), 3.65-3.77 (1H, m), 3.96-4.10 (1H, m), 4.23-4.42 (3H, m), 4.97 (1H, q, J=8.1Hz), 6.84 (1H, br.s), 7.22-7.62 (13H, m), 7.98-8.07 (2H, m);

MASS (ES+): m/e 771.52 (M+1).

Preparation 196

Compound (196) was obtained in a manner similar to Preparation 18.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.70 (3H, br.t, J=7.3Hz), 1.39 (3H, s), 1.54-2.21 (12H, m),2.86-3.39 (3H, m), 3.67-3.82 (1H, m), 4.18-4.38 (4H, m), 4.91-5.05 (1H, m), 7.23-7.54 (12H, m), 7.72 (1H, br-d, J=8.8Hz), 7.99 (2H, d, J=7.0Hz), 8.22 (2H, br.s), 8.42 (1H, br.s);

MASS (ES+): m/e 671.53 (free, M+1).

Preparation 197

Compound (197) was obtained in a manner similar to Preparation 76.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.82 (3H, t, J=7.3Hz), 1.28 (3H, s), 1.35-1.57 (2H, m), 1.64-2.00 (6H, m), 2.07-2.41 (4H, m), 3.01 (1H, dd, J=13.5, 6.3Hz), 3.21-3.38 (2H, m), 3.81-3.95 (1H, m), 4.19-4.31 (1H, m), 4.32 (2H, t, J=6.4Hz), 4.69 (1H, br-d, J=5.9Hz), 5.16-5.29 (1H, m), 5.93 (1H, s), 7.15 (1H, d, J=10.3Hz), 7.27-7.36 (4H, m), 7.38-7.47 (4H, m), 7.48-7.63 (5H, m), 8.03 (2H, d, J=7.3Hz);

MASS (ES+): m/e 653.45 (M+1).

Preparation 198

Compound (198) was obtained in a manner similar to Preparation 77.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.85 (3H, t, J=7.3Hz), 1.29 (3H, s), 1.30-1.95 (8H, m), 2.07-2.41 (4H, m), 3.01 (1H, dd, J=13.6 and 6.3Hz), 3.20-3.38 (2H, m), 3.66 (2H, t, J=6.3Hz), 3.82-3.95 (1H, m), 4.18-4.31 (1H, m), 4.70 (1H, br-d, J=5.9Hz), 5.16-5.29 (1H, m), 5.97 (1H, s), 7.14 (1H, d, J=10.6Hz), 7.24-7.65 (9H, m);

MASS (ES+): m/e 549.47 (M+1).

Preparation 199

Compound (199) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 93.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (3H, t, J=7.3Hz), 1.30 (3H, s), 1.52-1.94 (6H, m), 2.09-2.40 (4H, m), 2.51 (2H, br.t, J=6.2Hz), 3.01 (1H, dd, J=13.5 and 6.2Hz), 3.21-3.38 (2H, m), 3.83-3.95 (1H, m), 4.18-4.31 (1H, m), 4.69 (1H, br-d, J=5.4Hz), 5.16-5.29 (1H, m), 5.88 (1H, s), 7.14 (1H, d, J=10.2Hz), 7.24-7.37 (3H, m), 7.38-7.47 (2H, m), 7.48-7.60 (5H, m), 9.78 (1H, s);

MASS (ES+): m/e 547.44 (M+1).

Preparation 200

Compound (200) was obtained in a manner similar to Preparation 14.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.44 (3x3H, s), 1.53 (1H, m), 1.75-2.00 (3H, m), 2.65 (1H, m), 2.88 (1H, dd, J=13 and 10Hz), 3.02 (1H, dd, J=13 and 6Hz), 3.53 (1H, m), 3.85 (2x3H, s), 4.36 (1H, dd, J=8 and 4Hz), 4.62 (1H, ddd, J=10, 8 and 6Hz), 5.11 (1H, d, J=12Hz), 5.21 (1H, d, J=12Hz), 5.38 (1H, d, J=8Hz), 6.70-6.79 (3H, m), 7.28-7.40 (5H, m);

MASS (ES+): m/e 513.

Preparation 201

Compound (201) was obtained in a manner similar to Preparation 21.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.48 (1H, m), 1.70-1.90 (3H, m), 2.50 (1H, m), 3.11 (1H, m), 3.57 (1H, m), 3.72 (1H, m), 3.81 (3H, s), 3.84 (3H, s), 4.35 (1H, m), 4.66 (1H, m), 5.04 (1H, d, J=12Hz), 5.13 (1H, d, J=12Hz), 6.66-6.96 (3H, m), 7.22-7.37 (5H, m);

MASS (ES+): m/e 413.

Preparation 202

Compound (202) was obtained in a manner similar to Preparation 22.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.60 (3x1/7H, t, J=7.5Hz), 0.81 (3x6/7H, t, J=7.5Hz), 1.32 (3x1/7H, s), 1.39 (3x3x1/7H, s), 1.41 (3x6/7H, s), 1.43 (3x3x6/7H, s), 1.50-1.70 (2H, m), 1.76-2.02 (4H, m), 2.68 (1H, m), 2.88 (1H, dd, J=13.5 and 9.5Hz), 3.02 (1H, dd, J=13.5 and 5Hz), 3.56 (1H, m), 3.81 (3x1/7H, s), 3.82 (3x1/7H, s), 3.84 (3x6/7H, s), 3.85 (3x6/7H, s), 4.38 (1H, dd, J=8 and 4Hz), 4.92 (1H, ddd, J=9.5 and 8.5Hz), 5.11 (1H, d, J=12.5Hz), 5.13 (1H, br), 5.15 (1H, d, J=12.5Hz), 6.59-6.79 (3H, m), 6.88 (1H, d, J=8Hz), 7.28-7.40 (5H, m);

MASS (ES+): m/e 612.

Preparation 203

Compound (203) was obtained in a manner similar to Preparation 23.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.46 (3x1/3H, t, J=7.5Hz), 0.89 (3x2/3H, t, J=7.5Hz), 1.40-2.33 (6H, m), 1.50 (3x1/3H, s), 1.66 (3x2/3H, s), 2.85 (1x2/3H, m), 2.93-3.18 (2H, m), 3.50-3.90 (1+1/3H, m), 3.81 (3x1/3H, s), 3.83 (3x2/3H, s), 3.84 (3x2/3H, s), 3.85 (3x1/3H, s), 4.33 (1x2/3H, m), 4.67 (1/1/3H, m), 4.94 (1x2/3H, m), 5.07-5.34 (2+1/3H, m), 6.65-7.06 (3H, m), 7.23-7.41 (5H, m), 7.67 (1x2/3H, J=8Hz), 8.43 (1x1/3H, d, J=8Hz);

MASS (ES+): m/e 512.

Preparation 204

Compound (204) was obtained in a manner similar to Preparation 24.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.63 (3x1/8H, t, J=7.5Hz), 0.74 (3x7/8H, t, J=7.5Hz), 1.35 (3x1/8H, s), 1.42 (3x3x1/8H, s), 1.44 (3x3x7/8H, s9, 1.50 (3x7/8H, s), 2.76 (1H, m), 2.92 (1H, dd,

J=13.5 and 9Hz), 2.98 (1H, dd, J=13.5 and 5Hz), 3.57 (1H, m), 3.81 (2x3x1/8H, s), 3.84 (2x3x7/8H, s), 4.07 (1H, m), 4.32 (2H, t, J=6.5Hz), 4.38 (1H, dd, J=8.4Hz), 4.91 (1H, m), 5.13 (2H, s), 5.13 (1H, br), 6.59-6.83 (4H, m), 6.97 (1H, s), 7.28-7.40 (5H, m), 7.42 (2x1H, dd, J=7.5 and 7.5Hz);

MASS (ES+): m/e 845.

Preparation 205

Compound (205) was obtained in a manner similar to Preparation 25.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.78 (3H, t, J=7.5Hz), 1.36-2.24 (12H, m), 1.44 (3x4H, s), 2.78 (1H, m), 2.97 (2H, d, J=7Hz), 3.67 (1H, m), 3.80 (2x3H, s), 4.27-4.41 (3H, m), 4.91 (1H, dt, J=7.5 and 7Hz), 5.23 (1H, br), 6.71-6.80 (3H, m), 6.83 (1H, s), 7.28 (1H, d, J=7.5Hz), 7.43 (2x1H, dd, J=7.5 and 7.5Hz), 7.56 (1H, dd, J=7.5 and 7.5Hz), 8.03 (2x1H, d, J=7.5Hz);

MASS (ES+): m/e 753.

Preparation 206

Compound (206) was obtained in a manner similar to Preparation 18.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.73 (3H, br.t, J=7Hz), 1.40 (3H, s), 1.54-2.17 (12H, m), 2.80-3.08 (3H, m), 3.76 (1H, m), 3.81 (3H, s), 3.83 (3H, s), 4.20-4.40 (4H, m), 4.92 (1H, m), 6.68-6.82 (3H, m), 7.40 (2x1H, dd, J=7.5 and 7.5Hz), 7.53 (1H, dd, J=7.5 and 7.5Hz), 7.66 (1H, br-d, J=7Hz), 8.00 (2x1H, d, J=7.5Hz), 8.21 (2H, br), 8.36 (1H, br);

MASS (ES-): m/e 653.

Preparation 207

Compound (207) was obtained in a manner similar to Preparation 76.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.83 (3H, t, J=7.3Hz), 1.28 (3H, s), 1.47 (2H, m), 1.56-2.00 (6H, m), 2.06-2.40 (4H, m), 2.90 (1H, dd, J=13.5 and 6Hz), 3.20 (1H, dd, J=13.5 and 10Hz), 3.26 (1H, m), 3.85 (2x3H, s), 3.86 (1H, m), 4.24 (1H, dt, J=10 and 7.5Hz), 4.32 (2H, t, J=6.5Hz), 4.67 (1H, m), 5.16 (1H, ddd, J=10, 10 and 6Hz), 5.88 (1H, s), 6.75-6.80 (3H, m), 7.14 (1H, d, J=10Hz), 7.44 (2x1H, dd, J=7.5 and 7.5Hz), 7.52-7.60 (2H, m), 8.03 (2x1H, dd, J=7.5 and 1.5Hz);

MASS (ES+): m/e 637.

Preparation 208

Compound (208) was obtained in a manner similar to Preparation 76.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.82 (3H, t, J=7.3Hz), 1.28 (3H, s), 1,46 (2H, m), 1.62-2.06 (6H, m), 2.08-2.40 (4H, m), 2.90 (1H, dd, J=13.5 and 6Hz), 3.08-3.33 (2H, m), 3.85 (2x3H, s), 3.85 (1H, m), 4.24 (1H, m), 4.32 (1H, t, J=6.5Hz), 4.67 (1H, m), 5.15 (1H, m), 5.91 (1H, s), 6.74-6.80 (3H, m), 7.15 (1H, d, J=10Hz), 7.44 (2x1H, dd, J=7.5 and 7.5Hz), 7.52-7.62 (2H, m), 8.03 (2x1H, dd, J=7.5 and 1.5Hz);
MASS (ES-): m/e 635.

Preparation 209

Compound (209) was obtained in a manner similar to Preparation 77.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (3H, t, J=7.3Hz), 1.29 (3H, s), 1.30-1.53 (2H, m), 1.54-1.94 (6H, m), 2.07-2.40 (4H, m), 2.90 (1H, dd, J=13.5 and 6Hz), 3.19 (1H, dd, J=13.5 and 10Hz), 3.26 (1H, m), 3.66 (2H, t, J=6.5Hz), 3.85 (2x3H, s), 3.85 (1H, m), 4.22 (1H, dt, J=10 and 7.5Hz), 4.67 (1H, m), 5.15 (1H, ddd, J=10, 10 and 6Hz), 5.97 (1H, s), 6.74-6.80 (3H, m), 7.14 (1H, d, J=10Hz), 7.55 (1H, d, J=10Hz);
MASS (ES-): m/e 531.

Preparation 210

Compound (210) was obtained in a manner similar to Preparation 77.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.85 (3H, t, J=7.5Hz), 1.24-1.51 (2H, m), 1.29 (3H, s), 1.53-1.93 (6H, m), 2.08-2.40 (4H, m), 2.90 (1H, dd, J=13.5 and 6Hz), 3.19 (1H, dd, J=13.5 and 10Hz), 3.26 (1H, m), 3.66 (2H, t, J=6.5Hz), 3.85 (2x3H, s), 3.86 (1H, m), 4.23 (1H, dt J=10 and 7.5Hz), 4.68 (1H, m), 5.16 (1H, ddd, J=10, 10 and 6Hz), 6.03 (1H, s), 6.74-6.80 (3H, m), 7.15 (1H, d, J=10Hz), 7.56 (1H, d, J=10Hz);
MASS (ES-): m/e 531.

Preparation 211

Compound (211) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 96.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.85 (3H, t, J=7.3Hz), 1.30 (3H, s), 1.50-1.92 (6H, m), 2.08-2.40 (4H, m), 2.50 (2H, m), 2.90 (1H, dd, J=13.5 and 6Hz), 3.19 (1H, dd, J=13.5 and 9.5Hz), 3.25 (1H, m), 3.85 (2x3H, s), 3.86 (1H, m), 4.23 (1H, dt, J=10 and 7.3Hz), 4.67

(1H, dd, J=8 and 2.5Hz), 5.15 (1H, ddd, J=10, 9.5 and 6Hz), 5.93 (1H, s), 6.73-6.80 (3H, m), 7.16 (1H, d, J=10Hz), 7.50 (1H, d, J=10Hz), 9,77 (1H, t, J=1Hz);
MASS (ES-): m/e 529.

Preparation 212

Compound (212) was obtained in a manner similar to Preparation 14.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.74 (3x1/7H, d, J=7Hz), 0.80 (3x1/7H, t, J=7Hz), 0.89 (3x6/7H, t, J=7Hz), 0.94 (3x6/7H, d, J=7Hz), 1.12 (1H, m), 1.38-1.80 (3H, m), 1.42 (9x1/7H, s), 1.44 (9x6/7H, s), 1.88-2.26 (3H, m), 3.57 (1H, m), 3.90 (1H, m), 4.36 (1H, dd, J=9 and 7Hz), 4.49 (1H, dd, J=8 and 3Hz), 5.13 (1H, d, J=12.5Hz), 5.19 (1H, d, J=9Hz), 5.20 (1H, d, J=12.5Hz), 7.28-7.41 (5H, m);
MASS (ES+): m/e 419.

Preparation 213

Compound (213) was obtained in a manner similar to Preparation 21.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.70 (3x1/7H, t, J=7.3Hz), 0.75 (3x1/7H, d, J=7Hz), 0.86 (3x6/7H, t, J=7.3Hz), 0.98 (3x6/7H, d, J=7Hz), 1.13 (1H, m), 1.43 (1H, m), 1.76-2.02 (4H, m), 2.18 (1H, m), 3.52 (1H, m), 3.79 (1H, m), 4.13 (1H, m), 4.41 (1H, m), 5.10 (1x6/7H, d, J=12.5Hz), 5.12 (1x1/7H, d, J=12.5Hz), 5.19 (1x6/7H, d, J=12.5Hz), 5.22 (1x1/7H, d, J=12.5Hz), 7.30-7.44 (5H, m), 8.20 (2x6/7H, br), 8.32 (2x1/7H, br);
MASS (ES+): m/e 319.

Preparation 214

Compound (214) was obtained in a manner similar to Preparation 22.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.74 (3x1/5H, d, J=6.5Hz), 0.79 (3H, t, J=7.5Hz), 0.80 (3x1/5H, t, J=7.5Hz), 0.87 (3x4/5H, t, J=7.5Hz), 0.94 (3x4/5H, d, J=6.5Hz), 1.11 (1H, m), 1.39 (3H, s), 1.41 (9x1/5H, s), 1.43 (9x4.5H, s), 1.52-2.24 (8H, m), 3.57 (1H, m), 3.92 (1H, m), 4.32 (1x1/5H, dd, J=9.5 and 7.5Hz), 4.49 (1H, dd, J=8 and 3 Hz), 4.68 (1H, dd, J=9.5 and 7.5Hz), 5.13 (2H, s), 5.14 (1H, br), 6.58 (1x1/5H, d, J=9.5Hz), 6.67 (1x4/5H, d, J=9.5Hz), 7.24-7.40 (5H, m);
MASS (ES+): m/e 518.

Preparation 215

Compound (215) was obtained in a manner similar to

Preparation 23.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.71 (3x1/3H, d, J=6.5Hz), 0.77 (3x1/3H, t, J=7Hz), 0.82-0.99 (7H, m), 0.99-2.22 (9H, m), 1.63 (3x1/3H, s), 1.69 (3x2/3H, s), 3.56 (1H, m), 4.04 (1H, m), 4.28 (1x1/3H, dd, J=9.8Hz), 4.46 (1H, dd, J=8.3Hz), 4.63 (1x2/3H, dd, J=9 and 8Hz), 5.09-5.27 (2H, m), 7.25-7.40 (5H, m), 7.49 (1x2/3H, d, J=8Hz), 8.05 (1x1/3H, d, J=8Hz);
MASS (ES+): m/e 418.

Preparation 216

Compound (216) was obtained in a manner similar to Preparation 24.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.66-0.97 (9x1/5H, m), 0.72 (3x4/5H, t, J=7.3Hz), 0.87 (3x4/5H, t, J=7.4Hz), 0.93 (3x4/5H, d, J=6.7Hz), 1.00-2.45 (15H, m), 1.43 (3x3H, s), 1.50 (3x1/5H, s), 1.54 (3x4/5H, s), 3.57 (1H, m), 3.90 (1H, m), 4.08 (1H, m), 4.25-4.36 (2H, m), 4.59 (1H, dd, J=8 and 3Hz), 4.68 (1H, dd, J=9 and 8Hz), 5.02-5.24 (3H, m), 6.54 (1H, d, J=9Hz), 6.91 (1x1/5H, s), 7.07 (1x4/5H, s), 7.27-7.47 (7H, m), 7.55 (1H, m), 8.02 (2x1H, d, J=7Hz);
MASS (ES+): m/e 751.

Preparation 217

Compound (217) was obtained in a manner similar to Preparation 17.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.80 (3H, t, J=7.4Hz), 0.88 (3H, t, J=7.3Hz), 0.91 (3H, d, J=7.0Hz), 1.04-2.38 (15H, m), 3.56 (1H, m), 3.92-4.12 (2H, m), 4.26-4.38 (2H, m), 4.50 (1H, m), 4.60 (1H, dd, J=9, 8Hz), 5.28 (1H, br), 6.96 (1H, br-s), 7.15 (1H, br-d, J=9Hz), 7.43 (2x1H, dd, J=7.5 and 7.5Hz), 7.56 (1H, m), 8.03 (2x1H, dd, J=7.5 and 1.5Hz);
MASS (ES-): m/e 659.

Preparation 218

Compound (218) was obtained in a manner similar to Preparation 18.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.78-0.94 (9H, m), 1.02-2.22 (15H, m), 1.42 (3H, s), 3.52 (1H, m), 3.96 (1H, m), 4.20-4.40 (4H, m), 4.56 (1H, dd, J=9.8Hz), 7.35-7.57 (4H, m), 8.01 (2x1H, d, J=7.5Hz), 8.13 (2H, br), 8.36 (1H, br-s);
MASS (ES+): m/e 561.

Preparation 219

Compound (219) was obtained in a manner similar to Preparation 76.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.86 (3H, t, J=7Hz), 0.87 (3H, d, J=7Hz), 0.91 (3H, t, J=7Hz), 1.17 (2H, m), 1.29 (3H, s), 1.34-2.10 (9H, m), 2.11-2.42 (4H, m), 3.52 (1H, dt, J=10 and 7.5Hz), 3.89 (1H, ddd, J=10, 8.5 and 5Hz), 4.24 (1H, dt, J=10.5 and 7.5Hz), 4.31 (2H, t, J=7Hz), 4.56 (1H, dd, J=10.5 and 10.5Hz), 4.77 (1H, dd, J=8 and 2Hz), 5.86 (1H, s), 7.19 (1H, d, J=10.5Hz), 7.37 (1H, d, J=10.5Hz), 7.43 (2x1H, dd, J=7.5 and 7.5Hz), 7.56 (1H, m), 8.02 (2x1H, dd, J=7.5 and 1Hz);

MASS (ES+): m/e 543.

Preparation 220

Compound (220) was obtained in a manner similar to Preparation 77.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.86 (3H, d, J=7Hz), 0.88 (3H, t, J=7Hz), 0.91 (3H, t, J=7Hz), 1.08-1.51 (4H, m), 1.30 (3x3H, s), 1.53-1.76 (3H, m), 1.77-2.11 (4H, m), 2.13-2.43 (4H, m), 3.52 (1H, dt, J=10 and 7.5Hz), 3.65 (2H, t, J=7Hz), 3.89 (1H, ddd, J=10, 8.5 and 5Hz), 4.23 (1H, dt, J=10 and 7.5Hz), 4.58 (1H, dd, J=10.5 and 10.5Hz), 4.76 (1H, dd, J=7.5 and 2Hz), 6.01 (1H, s), 7.20 (1H, d, J=10Hz), 7.38 (1H, d, J=10.5Hz);

MASS (ES-): m/e 437.

Preparation 221

Compound (221) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 99.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.86 (3H, d, J=7Hz), 0.88 (3H, t, J=7Hz), 0.91 (3H, t, J=7Hz), 1.17 (2H, m), 1.31 (3H, s), 1.50-1.75 (3H, m), 1.74-2.10 (4H, m), 2.14-2.44 (4H, m), 2.49 (2H, m), 3.52 (1H, dt, J=10 and 7.5Hz), 3.89 (1H, ddd, J=10, 8.5 and 4.5Hz), 4.23 (1H, dt, J=10 and 7Hz), 4.58 (1H, dd, J=10.5 and 10.5Hz), 4.78 (1H, dd, J=8 and 2Hz), 5.91 (1H, s), 7.20 (1H, d, J=10Hz), 7.31 (1H, d, J=10Hz), 9.77 (1H, t, J=1Hz);

MASS (ES-): m/e 435.

Preparation 222

Compound (222) was obtained in a manner similar to Preparation 22.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.69 (3x1/5H, t, J=7Hz), 0.71 (3x1/5H, d, J=7Hz), 0.81 (3x4/5H, t, J=7Hz), 0.87 (3x4/5H, d, J=7Hz), 1.32-1.78 (4H, m), 1.39 (3x3H, s), 1.88-2.26 (3H, m), 2.82-3.10 (2H, m), 3.56 (1H, m), 3.77 (3x4/5H, s), 3.80 (3x1/5H, s), 3.92 (1H, m), 4.35 (1H, m), 4.48 (1H, dd, J=8 and 3Hz), 4.67 (1H, dd, J=9 and 7Hz), 4.94 (1H, m), 5.13 (1x4/5H, d, J=12.5Hz), 5.15 (1x1/5H, d, J=12Hz), 5.19 (1x4/5H, d, J=12.5Hz), 5.21 (1x1/5H, d, J=12Hz), 6.56 (1H, br-d, J=9Hz), 6.81 (2x1/5H, d, J=8.5Hz), 6.84 (2x4/5H, d, J=8.5Hz), 7.06 (2x1/5H, d, J=8.5Hz), 7.10 (2x4/5H, d, J=8.5Hz), 7.29-7.42 (5H, m);
MASS (ES+): m/e 596.

Preparation 223

Compound (223) was obtained in a manner similar to Preparation 23.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.49-0.60 (2H, m), 0.69-0.79 (4H, m), 0.79-0.98 (2H, m), 1.25 (1H, m), 1.66 (1H, m), 1.76-2.00 (2H, m), 2.17 (1H, m), 2.82-2.96 (1+1/3H, m), 3.04 (1x2/3H, dd, J=14 and 6Hz), 3.60 (1H, m), 3.70 (1H, m), 3.72 (3x1/3H, s), 3.73 (3x2/3H, s), 3.95 (1x1/3H, dd, J=9 and 8Hz), 4.00 (1x1/3H, m), 4.11 (1x2/3H, m), 4.36 (1H, dd, J=8.5 and 3.5Hz), 4.52 (1x2/3H, dd, J=9 and 8Hz), 5.09 (1x2/3H, d, J=12.5Hz), 5.12 (1x1/3H, d, J=12.5Hz), 5.13 (1x2/3H, d, J=12.5Hz), 5.24 (1x1/3H, d, J=12.5Hz), 6.87 (2x1/3H, d, J=8.5Hz), 6.90 (2x2/3H, d, J=8.5Hz), 7.16 (2x1/3H, d, J=8.5Hz), 7.24 (2x2/3H, d, J=8.5Hz), 7.30-7.44 (5H, m), 8.20 (2H, br), 8.73 (1x2/3H, d, J=9Hz), 8.82 (1x1/3H, d, J=9Hz);
MASS (ES+): m/e 496.

Preparation 224

Compound (224) was obtained in a manner similar to Preparation 24.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.64 (3x/6H, d, J=7Hz), 0.68 (3x1/6H, t, J=7Hz), 0.79 (3x5/6H, t, J=7Hz), 0.84 (3x5/6H, d, J=7Hz), 1.18-2.24 (13H, m), 3.00 (2H, m), 3.55 (1H, m), 3.75 (3H, s), 3.90 (1H, m), 4.08 (1H, m), 4.25 (2H, br-t, J=7Hz), 4.47 (1H, dd, J=8 and 2Hz), 4.56-4.71 (2H, m), 5.10 (1x5/6H, d, J=12.5Hz), 5.14 (1x1/6H, d, J=12.5Hz), 5.18 (1x5/6H, d, J=12.5Hz), 5.21 (1x1/6H, d, J=12.5Hz), 5.23 (1H, m), 6.45 (1H, br-d, J=9Hz), 6.67 (1H, d,

J=8Hz), 6.79 (2x1/6H, d, J=8.5Hz), 6.81 (2x5/6H, d, J=8.5Hz), 7.07 (2x1/6H, d, J=8.5Hz), 7.11 (2x5/6H, d, J=8.5Hz), 7.28-7.46 (7H, m), 7.54 (1H, m), 8.02 (2x/1H, d, J=7.5Hz);
MASS (ES+): m/e 829.

Preparation 225

Compound (225) was obtained in a manner similar to Preparation 17.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.78 (3H, t, J=7Hz), 0.84 (3H, d, J=6Hz), 1.16-2.24 (13H, m), 2.90-3.10 (2H, m), 3.54 (1H, m), 3.74 (3H, s), 3.92-4.19 (2H, m), 4.28 (2H, m), 4.40-4.52 (2H, m), 4.65 (1H, m), 5.40 (1H, br-d, J=7.5Hz), 6.78 (2x1H, d, J=8.5Hz), 6.86 (1H, br-d, J=8Hz), 6.94 (1H, br-d, J=8Hz), 7.11 (2x1H, br-d, J=8.5Hz), 7.42 (2x1H, dd, J=7.5 and 7.5Hz), 7.55 (1H, dd, J=7.5 and 7.5Hz), 8.02 (2x1H, d, J=7.5Hz);
MASS (ES-): m/e 737.

Preparation 226

Compound (226) was obtained in a manner similar to Preparation 18.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.74 (3H, t, J=7Hz), 0.88 (3H, d, J=6.5Hz), 1.02 (1H, m), 1.20-1.46 (4H, m), 1.60-2.18 (8H, m), 2.91 (1H, dd, J=13.5 and 8Hz), 3.08 (1H, dd, J=13.5 and 6.5Hz), 3.48 (1H, m), 3.96 (1H, m), 4.14-4.35 (5H, m), 5.03 (1H, m), 6.67 (2x1H, d, J=8.5Hz), 7.26 (2x1H, d, J=8.5Hz), 7.40 (2x1H, dd, J=7.5 and 7.5Hz), 7.52 (1H, dd, J=7.5 and 7.5Hz), 8.02 (2x1H, d, J=7.5Hz), 8.04 (2H, br), 8.20 (1H, br), 8.47 (1H, br);
MASS (ES-): m/e 637.

Preparation 227

Compound (227) was obtained in a manner similar to Preparation 76.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (3H, d, J=7Hz), 0.86 (3H, t, J=7Hz), 1.09 (1H, m), 1.31-2.02 (10H, m), 2.24-2.46 (6H, m), 2.78 (1H, dd, J=14 and 7.5Hz), 3.15 (1H, dd, J=14 and 7.5Hz), 3.51 (1H, m), 3.76 (3H, s), 4.02 (1H, m), 4.22-4.34 (3H, m), 4.48 (1H, dd, J=10.5 and 10.5Hz), 4.64-4.76 (2H, m), 6.25 (1H, d, J=10Hz), 6.28 (1H, d, J=10.5Hz), 6.79 (2x1H, d, J=8.5Hz), 7.11 (2x1H, d, J=8.5Hz), 7.22 (1H, d, J=10Hz), 7.44 (2x1H, dd, J=7.5 and 7.5Hz), 7.56 (1H, m), 8.02 (2x1H, dd, J=7.5 and 1.5Hz);

MASS (ES-): m/e 619.

Preparation 228

Compound (228) was obtained in a manner similar to Preparation 77.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (3H, d, J=6.5Hz), 0.86 (3H, t J=7Hz), 1.10 (1H, m), 1.22-2.02 (10H, m), 2.24-2.46 (2H, m), 2.79 (1H, dd, J=14.5 and 7.5Hz), 3.15 (1H, dd, J=14.5 and 7.5Hz), 3.51 (1H, m), 3.61 (2H, br-t, J=6Hz), 3.78 (3H, s), 4.02 (1H, m), 4.27 (1H, dt, J=10 and 7.5Hz), 4.48 (1H, dd, J=10.5 and 10Hz), 4.64-4.76 (2H, m), 6.31 (1H, d, J=10.5Hz), 6.38 (1H, d, J=10Hz), 6.81 (2x1H, d, J=8.5Hz), 7.12 (2x1H, d, J=8.5Hz), 7.22 (1H, d, J=10Hz);

MASS (ES-): m/e 515.

Preparation 229

Compound (229) was obtained in a manner similar to Preparation 78.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (3H, t, J=6.6Hz), 0.86 (3H, t, J=7.3Hz), 1.09 (1H, m), 1.20-2.02 (10H, m), 2.24-2.46 (2H, m), 2.79 (1H, dd, J=14.3 and 7.9Hz), 3.15 (1H, dd, J=14.3 and 7.3Hz), 3.51 (1H, m), 3.61 (2H, t, J=6.4Hz), 3.78 (3H, s), 4.02 (1H, m), 4.27 (1H, dt, J=10.3 and 7.6Hz), 4.48 (1H, dd, J=11.0 and 10.5Hz), 4.69 (1H, ddd, J=9.9, 7.9 and 7.3Hz), 4.72 (1H, dd, J=8.0 and 2.0Hz), 6.31 (1H, d, J=10.5Hz), 6.37 (1H, d, J=9.9Hz), 6.81 (2x1H, d, J=8.4Hz), 7.12 (2x1H, d, J=8.4Hz), 7.22 (1H, d, J=10.3Hz);

MASS (ES-): m/e 515.

Preparation 230

Compound (230) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 102.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.85 (3H, d, J=6.6Hz), 0.87 (3H, t, J=7.3Hz), 1.10 (1H, m), 1.44-2.06 (8H, m), 2.25-2.54 (4H, m), 2.80 (1H, dd, J=14.5 and 8Hz), 3.16 (1H, dd, J=14.5 and 7.7Hz), 3.52 (1H, m), 4.03 (1H, m), 4.28 (1H, dt, J=10 and 7Hz), 4.49 (1H, dd, J=10.7 and 10.6Hz), 4.69 (1H, ddd, J=9.8, 8 and 7.7Hz), 4.74 (1H, m), 6.28 (1H, d, J=10.6Hz), 6.32 (1H, d, J=9.8Hz), 6.81 (2x1H, d, J=8.7Hz), 7.12 (2x1H, d, J=8.7Hz), 7.24 (1H, d, J=10Hz), 9.73 (1H, s);

MASS (ES-): m/e 513.

Preparation 231

Compound (231) was obtained in a manner similar to Preparation 24.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.27-1.97 (10H, m), 1.41 (9x1/6H, s), 1.43 (9x5/6H, s), 2.64 (1H, m), 2.70-3.08 (4H, m), 3.56 (1H, m), 3.71 (3x1/6H, s), 3.73 (3x5/6H, s), 4.06 (1H, m), 4.27 (2H, br-t, J=7Hz), 4.31 (1H, dd, J=8 and 4Hz), 4.68 (1H, m), 4.90 (1H, m), 5.10 (1H, d, J=12Hz), 5.16 (1H, d, J=12Hz), 5.18 (1H, d, J=7Hz), 6.68 (2x1/6H, d, J=8.5Hz), 6.73-6.92 (2H, m), 6.80 (2x5/6H, d, J=8.5Hz), 7.08 (2H, d, J=8.5Hz), 7.12-7.38 (9H, m), 7.42 (2H, dd, J=7.5 and 7.5Hz), 7.55 (1H, dd, J=7.5 and 7.5Hz), 8.03 (2H, d, J=7.5Hz);

MASS (ES+): m/e 863.

Preparation 232

Compound (232) was obtained in a manner similar to Preparation 17.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.18-2.14 (10H, m), 1.41 (3x3H, s), 2.36 (3H, s), 2.68 (1H, m), 2.84-3.10 (4H, m), 3.72 (1H, m), 3.74 (3H, s), 4.06 (1H, m), 4.22-4.36 (3H, m), 4.70 (1H, m), 4.81 (1H, m), 5.29 (1H, br-d, J=7.5Hz), 6.78 (2x1H, d, J=8.5Hz), 6.92 (1H, br), 7.04 (2x1H, br-d, J=8.5Hz), 7.14-7.32 (5H, m), 7.42 (2x1H, dd, J=7.5 and 7.5Hz), 7.48-7.60 (2H, m), 8.02 (2x1H, dd, J=7.5 and 1.5Hz);

MASS (ES-): m/e 771.

Preparation 233

Compound (233) was obtained in a manner similar to Preparation 18.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.12-1.98 (10H, m), 2.70-2.90 (2H, m), 2.91-3.12 (3H, m), 3.65 (3H, s), 4.07-4.34 (4H, m), 4.58 (1H, m), 5.07 (1H, m), 6.75 (2x1H, d, J=8.5Hz), 7.13-7.30 (7H, m), 7.40 (2x1H, dd, J=7.5 and 7.5Hz), 7.52 (1H, dd, J=7.5 and 7.5Hz), 7.98-8.12 (2H, br), 8.02 (2x1H, d, J=7.5Hz);

MASS (ES-): m/e 671.

Preparation 234

Compound (234) was obtained in a manner similar to Preparation 76.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.44 (2H, m), 1.66-1.96 (6H, m), 2.13-2.40 (2H, m), 2.77 (1H, dd, J=14 and 7Hz), 2.87 (1H, dd, J=13 and 5Hz), 3.02-3.24 (3H, m), 3.77 (3H, s), 3.94 (1H, m), 4.24-4.35 (2H, m), 4.61 (1H, dd, J=8 and 2.5Hz), 4.69 (1H, m), 5.06 (1H, ddd, J=10, 10 and 5Hz), 6.24 (1H, d, J=10Hz), 6.44 (1H, d, J=10Hz), 6.81 (2x1H, d, J=8.5Hz), 7.09-7.32 (8H, m), 7.44 (2x1H, dd, J=7.5 and 7.5Hz), 7.56 (1H, m), 8.03 (2H, dd, J=7.5 and 1.5Hz);
MASS (ES-) m/e 653.

Preparation 235

Compound (235) was obtained in a manner similar to Preparation 77.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.24-1.91 (8H, m), 2.10-2.40 (2H, m), 2.78 (1H, dd, J=14 and 7Hz), 2.87 (1H, dd, J=13.5 and 5.5Hz), 3.02-3.24 (3H, m), 3.63 (2H, br-t, J=6Hz), 3.78 (3H, s), 3.94 (1H, m), 4.28 (1H, dt, J=10 and 8Hz), 4.61 (1H, dd, J=8 and 3Hz), 4.69 (1H, m), 5.06 (1H, ddd, J=10, 10 and 5.5Hz), 6.35 (1H, d, J=10Hz), 6.46 (1H, d, J=10Hz), 6.82 (2x1H, d, J=8.5Hz), 7.09-7.32 (8H, m);
MASS (ES-): m/e 549.

Preparation 236

Compound (236) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 105.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.48-1.90 (4H, m), 2.10-2.50 (4H, m), 2.78 (1H, dd, J=14 and 7Hz), 2.87 (1H, dd, J=13.5 and 5Hz), 3.07 (1H, m), 3.16 (1H, dd, J=14 and 8.5Hz), 3.18 (1H, dd, J=13.5 and 11Hz), 3.78 (3H, s), 3.94 (1H, m), 4.28 (1H, dt, J=10.3 and 7.3Hz), 4.62 (1H, dd, J=8 and 2.5Hz), 4.68 (1H, ddd, J=10, 8.5 and 7Hz), 5.06 (1H, ddd, J=11, 10 and 5Hz), 6.32 (1H, d, J=10Hz), 6.82 (2x1H, d, J=9Hz), 7.09-7.32 (8H, m), 9.74 (1H, t, J=1Hz);
MASS (ES-): m/e 547.

Preparation 237

Compound (237) was obtained in a manner similar to Preparation 14.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.40 (3x3H, s), 1.80 (1H, m), 1.90-2.11 (3H, m), 3.12 (1H, m), 3.73 (1H, m), 4.48 (1H, m), 5.17 (1H, d, J=12Hz), 5.23 (1H, d, J=12Hz), 5.43 (1H, d, J=7Hz), 6.12 (1H,

d, J=7Hz), 7.23-7.45 (10H, m);
MASS (ES+): m/e 439.

Preparation 238

Compound (238) was obtained in a manner similar to Preparation 21.

[1]H-NMR (300MHz, $CDCl_3$, δ): 1.72-2.10 (4H, m), 2.71 (1H, m), 3.82 (1H, m), 4.46 (1H, m), 5.12 (1H, dd, J=12.5Hz), 5.22 (1H, dd, J=12.5Hz), 5.50 (1H, s), 7.30-7.54 (10H, m), 8.66 (2H, br-s);
MASS (ES+): m/e 339.

Preparation 239

Compound (239) was obtained in a manner similar to Preparation 22.

[1]H-NMR (300MHz, $CDCl_3$, δ): 0.71 (3H, t, J=7.5Hz), 1.36 (3x3H, br-s), 1.42 (3H, s), 1.56-2.10 (6H, m), 3.11 (1H, m), 3.74 (1H, m), 4.49 (1H, m), 5.16 (2H, s), 5.64 (1H, d, J=6.5Hz), 7.21-7.43 (11H, m), 7.63 (1H, d, J=6.5Hz);
MASS (ES+): m/e 538.

Preparation 240

Compound (240) was obtained in a manner similar to Preparation 23.

[1]H-NMR (300MHz, $CDCl_3$, δ): 0.95 (3H, t, J=7Hz), 1.60 (3H, s), 1.70-2.19 (6H, m), 3.09 (1H, m), 3.78 (1H, m), 4.48 (1H, m), 5.16 (2H, s), 5.73 (1H, d, J=6.5Hz), 7.22-7.45 (10H, m), 7.62 (1H, d, J=6.5Hz), 8.02 (2H, br-s);
MASS (ES+): m/e 438.

Preparation 241

Compound (241) was obtained in a manner similar to Preparation 24.

[1]H-NMR (300MHz, $CDCl_3$, δ): 0.72 (3H, t, J=7.5Hz), 1.36-2.42 (12H, m), 1.41 (3x3H, s), 1.47 (3H, s), 3.11 (1H, m), 3.73 (1H, m), 4.04 (1H, m), 4.28 (2H, t, J=6Hz), 4.50 (1H, m), 5.07 (1H, br), 5.16 (1H, d, J=12.5Hz), 5.19 (1H, d, J=12.5Hz), 5.62 (1H, d, J=6Hz), 7.03 (1H, s), 7.26-7.48 (13H, m), 7.54 (1H, m), 8.01 (2x1H, dd, J=7, 1.5Hz);
MASS (ES+): m/e 793 (M+Na).

Preparation 242

Compound (242) was obtained in a manner similar to Preparation 17.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.68 (3H, br-t, J=7Hz), 1.34-2.21 (12H, m), 1.42 (3x3H, s), 1.44 (3H, s), 3.12 (1H, m), 3.77 (1H, m), 4.05 (1H, m), 4.33 (2H, br-t, J=6Hz), 4.46 (1H, m), 5.14 (1H, br), 5.67 (1H, d, J=7Hz), 6.89 (1H, br-s), 7.24-7.47 (7H, m), 7.56 (1H, m), 7.69 (1H, br-d, J=7Hz), 8.03 (2x1H, dd, J=7.5 and 1Hz);

MASS (ES-): m/e 679.

^{1}H-NMR (300MHz, DMSO-d_6, δ): 0.57 (3x7/9H, t, J=7.5Hz), 0.62 (3x2/9H, t, J=7.5Hz), 1.26-2.08 (12H, m), 1.33 (3H, s), 1.34 (3x3H, s), 3.12 (1H, m), 3.75 (1H, m), 3.88 (1H, m), 4.19-4.32 (3H, m), 5.58 (1x2/9H, d, J=7.5Hz), 5.68 (1x7/9H, d, J=7.5Hz), 6.94 (1H, d, J=8.5Hz), 7.22-7.41 (5H, m), 7.52 (2x1H, dd, J=7.5, 7.5Hz), 7.66 (1H, m), 7.78 (1H, s), 7.96 (2x1H, dd, J=7.5 and 1.5Hz).

Preparation 243

Compound (243) was obtained in a manner similar to Preparation 18.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.70 (3H, t, J=7Hz), 1.42 (3H, s), 1.54-2.16 (12H, m), 3.09 (1H, m), 3.83 (1H, m), 4.26-4.54 (4H, m), 5.77 (1H, d, J=7Hz), 7.25-7.42 (7H, m), 7.51 (1H, dd, J=7.5 and 7.5Hz), 7.58 (1H, br), 7.91 (2H, br-s), 8.02 (2x1H, d, J=7.5Hz), 8.62 (1H, s);

MASS (ES+): m/e 581.

^{1}H-NMR (300MHz, DMSO-d_6, δ): 0.59 (3H, t, J=7.5Hz), 1.32-1.92 (12H, m), 1.37 (3H, s), 3.07 (1H, m), 3.74 (1H, m), 3.88 (1H, m), 1.25 (1H, dd, J=8, 2Hz), 4.30 (2H, t, J=6Hz), 5.65 (1H, d, J=7Hz), 7.25-7.40 (5H, m), 7.52 (1H, dd, J=7.5 and 7.5Hz), 7.66 (1H, m), 7.90 (2H, d, J=7Hz), 7.98 (2x1H, dd, J=7.5 and 1.5Hz), 8.15 (2H, br), 8.40 (1H, s).

Preparation 244

Compound (244) was obtained in a manner similar to Preparation 76.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.90 (3H, t, J=7.3Hz), 1.36 (3H, s), 1.48 (2H, m), 1.58-2.56 (10H, m), 3.76 (1H, m), 4.04 (1H, m), 4.30 (1H, m), 4.32 (2H, t, J=6.5Hz), 4.76 (1H, m), 5.99 (1H, s), 6.20 (1H, d, J=10Hz), 7.17 (1H, d, J=10Hz), 7.28-7.49 (7H, m), 7.56 (1H, m), 8.04 (2H, m), 8.10 (1H, d, J=10Hz);

MASS (ES+): m/e 563.

Preparation 245

Compound (245) was obtained in a manner similar to Preparation 77.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.92 (3H, t, J=7.5Hz), 1.36 (3H, s), 1.39 (2H, m), 1.52-1.71 (4H, m), 1.79-2.06 (3H, m), 2.10-2.53 (4H, m), 3.65 (1H, dt, J=6 and 6Hz), 3.74 (1H, m), 4.04 (1H, m), 4.27 (1H, dt, J=10 and 7.5Hz), 4.75 (1H, dd, J=8, 2Hz), 5.97 (1H, s), 6.19 (1H, d, J=10.5Hz), 7.14 (1H, d, J=10Hz), 7.28-7.43 (5H, m), 8.08 (1H, d, J=10.5Hz);

MASS (ES+): m/e 459.

Preparation 246

Compound (246) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 108.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.92 (3H, t, J=7.4Hz), 1.26 (3H, s), 1.52-1.74 (3H, m), 1.78-2.06 (3H, m), 2.12-2.54 (6H, m), 3.74 (1H, dt, J=10 and 7Hz), 4.04 (1H, m), 4.28 (1H, dt, J=10.5 and 7Hz), 4.76 (1H, dd, J=8 and 2Hz), 6.05 (1H, s), 6.18 (1H, d, J=10Hz), 7.18 (1H, d, J=10Hz), 7.28-7.42 (5H, m), 8.02 (1H, d, J=10Hz), 9.77 (1H, br-s);

MASS (ES-): m/e 455.

Preparation 247

Compound (247) was obtained in a manner similar to Preparation 20.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.60-2.30 (17H, m), 1.41 (9x1/4H, s), 1.44 (9x3/4H, s), 3.42-3.64 (1H, m), 3.84 (1H, m), 4.27 (1x1/4H, m), 4.47 (1x3/4H, m), 4.58 (1H, m), 4.97 (1H, m), 5.13 (1H, d, J=12.5Hz), 5.13-5.23 (1H, m), 5.19 (1H, d, J=12.5Hz), 7.28-7.42 (5H, m);

MASS (ES+): m/e 459.

Preparation 248

Compound (248) was obtained in a manner similar to Preparation 21.

^{1}H-NMR (300MHz, DMSO-d_6, δ): 0.68-1.34 (5H, m), 1.38-1.76 (7H, m), 1.82-2.06 (4H, m), 2.18 (1H, m), 3.42 (1H, m), 3.80 (1H, m), 4.25 (1H, br-t, J=6Hz), 4.39 (1H, dd, J=8.5 and 2.5Hz), 5.10 (1H, d, J=12.5Hz), 5.18 (1H, d, J=12.5Hz), 7.13-7.44 (5H, m), 8.20

(2H, br-s); MASS (ES+): m/e 359.

Preparation 249

Compound (249) was obtained in a manner similar to Preparation 22.

^{1}H-NMR (300MHz, DMSO-d_6, δ): 0.68 (3x2/3H, br-t, J=7Hz), 0.77-2.30 (19H, m), 0.84 (3x1/3H, br-t, J=7Hz), 1.24 (3x1/3H, s), 1.27 (3x2/3H, s), 1.33 (9x1/3H, s), 1.36 (9x2/3H, s), 3.50 (1H, m), 3.69 (1H, m), 4.31 (1H, dd, J=8 and 3Hz), 4.42 (1x1/3H, m), 4.69 (1x2/3H, m), 5.03 (1H, d, J=12.5Hz), 5.10 (1H, d, J=12.5Hz), 6.54 (1x1/3H, br), 6.67 (1x2/3H, br), 7.31-7.42 (5H, m), 7.44 (1x1/3H, d, J=8Hz), 7.70 (1x2/3H, d, J=8Hz);

MASS (ES+): m/e 558.

Preparation 250

Compound (250) was obtained in a manner similar to Preparation 23.

^{1}H-NMR (300MHz, DMSO-d_6, δ): 0.74 (3x1/4H, t, J=7.5Hz), 0.78 (3x3/4H, t, J=7.5Hz), 0.82-2.28 (19H, m), 1.44 (3x1/4H, s), 1.47 (3x3/4H, s), 3.56 (1H, m), 3.77 (1H, m), 4.33 (1H, dd, J=8.5 and 3Hz), 4.78 (1x3/4H, m), 5.01 (1H, d, J=12.5Hz), 5.04 (1x1/4H, m), 5.16 (1H, d, J=12.5Hz), 7.29-7.42 (5H, m), 8.15 (2H, br-s), 8.46 (1x3/4H, d, J=8.5Hz), 8.62 (1x1/4H, d, J=8.5Hz);

MASS (ES+): m/e 458.

Preparation 251

Compound (251) was obtained in a manner similar to Preparation 24.

^{1}H-NMR (300MHz, DMSO-d_6, δ): 0.57 (3H, t, J=7.3Hz), 0.70-2.30 (25H, m), 1.34 (3H, s), 1.36 (3x3H, s), 3.52 (1H, m), 3.66-3.84 (2H, m), 4.24 (2H, t, J=6.5Hz), 4.31 (1H, dd, J=9 and 3Hz), 4.76 (1H, m), 5.01 (1H, d, J=12.5Hz), 5.12 (1H, d, J=12.5Hz), 7.14 (1H, m), 7.29-7.42 (5H, m), 7.51 (2H, m), 7.65 (1H, m), 7.70 (1H, s), 7.80 (1H, d, J=6.5Hz), 7.95 (2x1H, d, J=7Hz);

MASS (ES+): m/e 791.

Preparation 252

Compound (252) was obtained in a manner similar to Preparation 17.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.76-2.36 (25H, m), 0.80 (3H, t, J=7.5Hz), 1.43 (3x3H, s), 1.48 (3H, s), 3.50 (1H, m), 3.93 (1H,

m), 4.02 (1H, m), 4.33 (2H, t, J=6.5Hz), 4.59 (1H, m), 4.86 (1H, m), 5.23 (1H, m), 6.91 (1H, s), 7.16 (1H, d, J=8.5Hz), 7.43 (2x1H, dd, J=8 and 8Hz), 7.56 (1H, m), 8.03 (2x1H, dd, J=8 and 1.5Hz);
MASS (ES-): m/e 699.

Preparation 253

Compound (253) was obtained in a manner similar to Preparation 18.
^{1}H-NMR (300MHz, DMSO-d_6, δ): 0.67 (3x1/2H, t, J=7.5Hz), 0.68 (3x1/2H, t, J=7.5Hz), 0.72-2.32 (25H, m), 1.40 (3x1/2H, s), 1.41 (3x1/2H, s), 3.33 (1H, m), 3.48 (1x1/2H, m), 3.71 (1x1/2H, m), 3.96 (1H, m), 4.18 (1x1/2H, dd, J=8.5 and 2.5Hz), 4.27 (2x1/2H, t, J=6.2Hz), 4.29 (2x1/2H, t, J=6.2Hz), 4.42 (1x1/2H, m), 4.75 (1x1/2H, m), 4.81 (1x1/2H, d, J=8 and 2Hz), 7.53 (2x1/2H, dd, J=7.5 and 7.5Hz), 7.67 (1H, dd, J=7.5 and 7.5Hz), 7.75 (1x1/2H, d, J=8.5Hz), 7.88 (1x1/2H, d, J=8.5Hz), 7.96 (2x1H, d, J=7.5Hz), 8.05 (2H, br), 8.14 (1x1/2H, s), 8.16 (1x1/2H, s);
MASS (ES+): m/e 601.

Preparation 254

Compound (254) was obtained in a manner similar to Preparation 76.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.85 (3H, t, J=7Hz), 0.96 (2H, m), 1.08-1.26 (4H, m), 1.28 (3H, s), 1.45 (2H, m), 1.55-1.98 (13H, m), 2.07-2.42 (4H, m), 3.52 (1H, m), 3.96 (1H, m), 4.24 (1H, ddd, J=10, 8 and 8Hz), 4.31 (2H, t, J=6Hz), 4.74 (1H, m), 5.00 (1H, ddd, J=10, 8 and 8Hz), 5.83 (1H, s), 7.14 (1H, d, J=10Hz), 7.34 (1H, d, J=10Hz), 7.43 (2x1H, dd, J=7.5 and 7.5Hz), 7.56 (1H, dd, J=7.5 and 7.5Hz), 8.03 (2x1H, d, J=7.5Hz);
MASS (ES-): m/e 581.

Preparation 255

Compound (255) was obtained in a manner similar to Preparation 77.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.87 (3H, t, J=7.3Hz), 0.96 (2H, m), 1.08-1.51 (6H, m), 1.53-2.00 (11H, m), 2.09-2.43 (4H, m), 3.51 (1H, ddd, J=10, 7.5 and 7Hz), 3.65 (2H, br-t, J=5Hz), 3.96 (1H, m), 4.23 (1H, ddd, J=10, 8 and 7Hz), 4.74 (1H, dd, J=8 and 2Hz), 4.99 (1H, ddd, J=10, 8 and 8Hz), 6.01 (1H, s), 7.16 (1H, d,

J=10Hz), 7.35 (1H, d, J=10Hz);
MASS (ES-): m/e 477.

Preparation 256

Compound (256) was obtained in a manner similar to Preparation 78. The obtained compound was used in Examples 111 and 114.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.87 (3H, t, J=7.3Hz), 0.96 (2H, m), 1.08-1.35 (4H, m), 1.30 (3H, s), 1.50-2.02 (13H, m), 2.10-2.44 (4H, m), 2.49 (2H, m), 3.52 (1H, dt, J=10 and 7.3Hz), 3.96 (1H, m), 4.23 (1H, ddd, J=10, 7.5 and 7Hz), 4.74 (1H, dd, J=8 and 2Hz), 4.99 (1H, dt, J=10 and 7.5Hz), 5.89 (1H, s), 7.16 (1H, d, J=10Hz), 7.29 (1H, d, J=10Hz), 9.76 (1H, t, J=1Hz);
MASS (ES-): m/e 475.

Preparation 257

Compound (257) was obtained in a manner similar to Preparation 22.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.18-2.18 (14H, m), 1.41 (9x3/4H, s), 1.48 (9x1/4H, s), 2.64 (1H, m), 2.88 (1H, m), 3.03 (1x3/4H, m), 3.15 (1x1/4H, m), 3.50 (1x3/4H, m), 3.58 (1x1/4H, m), 4.17 (1H, dd, J=8 and 3.5Hz), 4.68-5.14 (3H, m), 6.86-7.44 (12H, m);
MASS (ES+): m/e 578.

Preparation 258

Compound (258) was obtained in a manner similar to Preparation 23.

^{1}H-NMR (300MHz, DMSO-d_6, δ): 0.82-2.14 (14H, m), 1.35 (9x5/6H, s), 1.45 (9x5/6H, s), 2.83 (1H, dd, J=13 and 5Hz), 2.92 (1H, dd, J=13 and 6.5Hz), 3.17 (1H, m), 3.40 (1x1/6H, m), 3.53 (1x5/6H, m), 4.06 (1x5/6H, dd, J=8.5 and 3.5Hz), 4.47 (1x1/6H, m), 4.73 (1x5/6H, m), 4.84 (1x1/6H, m), 7.11-7.30 (5H, m), 8.30 (1H, d, J=8.5Hz);
MASS (ES+): m/e 444.

Preparation 259

Compound (259) was obtained in a manner similar to Preparation 24.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.12-2.28 (20H, m), 1.42 (3x3H, s), 1.44 (3x3H, s), 2.69 (1H, m), 2.92 (1H, dd, 1=13.5 and 9.5Hz), 3.03 (1H, dd, J=13.5 and 5Hz), 3.51 (1H, m), 3.93-4.20 (2H, m), 4.33 (2H, br-t, J=6Hz), 4.88 (1H, m), 5.17 (1H, br), 6.51 (1H,

br-s), 7.12-7.32 (6H, m), 7.44 (2x1H, dd, J=7.5 and 7.5Hz), 7.56 (1H, dd, J=7.5 and 7.5Hz), 8.03 (2x1H, d, J=7.5Hz);
MASS (ES-): m/e 775.

Preparation 260

Compound (260) was obtained in a manner similar to Preparation 57.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.06-2.10 (19H, m), 2.32 (1H, m), 2.87-3.07 (3H, m), 3.74 (1H, m), 4.08-4.42 (4H, m), 4.74 (1H, m), 7.14-7.32 (6H, m), 7.38-7.62 (4H, m), 7.77 (2H, br), 8.02 (2x1H, d, J=8Hz);
MASS (ES+): m/e 620.

Preparation 261

Compound (261) was obtained in a manner similar to Preparation 76.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.26-1.96 (16H, m), 2.04 (1H, m), 2.17 (1H, m), 2.30 (1H, m), 2.62 (1H, m), 2.95 (1H, dd, J=13.6Hz), 3.21 (1H, m), 3.25 (1H, dd, J=13 and 10Hz), 3.92 (1H, m), 4.25 (1H, ddd, J=10, 8 and 7.5Hz), 4.32 (2H, t, J=6.5Hz), 4.66 (1H, m), 5.16 (1H, ddd, J=10, 10 and 6Hz), 5.70 (1H, s), 7.15-7.32 (6H, m), 7.38 (1H, d, J=10Hz), 7.44 (2H, m), 7.56 (1H, m), 8.03 (2H, m);
MASS (ES-): m/e 601.

Preparation 262

Compound (262) was obtained in a manner similar to Preparation 77.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.22-1.93 (16H, m), 2.04 (1H, m), 2.16 (1H, m), 2.30 (1H, m), 2.63 (1H, m), 2.95 (1H, dd, J=13.5 and 6Hz), 3.20 (1H, m), 3.26 (1H, dd, J=13.5 and 10Hz), 3.66 (2H, t, J=6.5Hz), 3.92 (1H, m), 4.24 (1H, ddd, J=10, 8 and 8Hz), 4.64 (1H, m), 5.16 (1H, ddd, J=10, 10 and 6Hz), 5.84 (1H, s), 7.15-7.32 (6H, m), 7.38 (1H, d, J=10Hz);
MASS (ES-): m/e 497.

Preparation 263

Compound (263) was obtained in a manner similar to Preparation 78. The obtained compound was used in Examples 117 and 120.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.20-1.93 (14H, m), 1.98-2.67 (6H, m), 2.95 (1H, dd, J=14 and 5Hz), 3.20 (1H, m), 3.24 (1H, dd, J=14 and

10Hz), 3.92 (1H, m), 4.24 (1H, m), 4.66 (1H, m), 5.16 (1H, ddd, J=10, 5 and 5Hz), 5.76 (1H, s), 7.15-7.40 (7H, m), 9.77 (1H, t, J=1Hz);

MASS (ES-): m/e 495.

Preparation 264

Compound (262) was obtained in a manner similar to Preparation 77. The obtained compound was used in Examples 117 and 120.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.24-1.90 (14H, m), 1.96-2.25 (2H, m), 2.32 (1H, m), 2.50 (2H, m), 2.60 (1H, m), 2.95 (1H, dd, J=13.5 and 6Hz), 3.20 (1H, m), 3.24 (1H, dd, J=13.5 and 10Hz), 3.93 (1H, m), 4.24 (1H, m), 4.66 (1H, dd, J=8 and 2.5Hz), 5.16 (1H, ddd, J=10, 10 and 6Hz), 5.76 (1H, s), 7.16-7.34 (6H, m), 7.34 (1H, d, J=10Hz), 9.77 (1H, t, J=1Hz);

MASS (ES-): m/e 495.

Preparation 265

Compound (265) was obtained in a manner similar to Preparation 21.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.52 (1H, m), 1.66-2.01 (3H, m), 2.71 (1H, m), 2.96 (1H, dd, J=13.5 and 8Hz), 3.14 (1H, dd, J=13.5 and 6Hz), 3.55 (1H, m), 4.26 (1H, dd, J=8.5 and 3.5Hz), 4.41 (1H, br), 5.08 (1H, d, J=12.5Hz), 5.19 (1H, d, J=12.5Hz), 7.16-7.46 (10H, m), 8.41 (2H, br-s);

MASS (ES+): m/e 353.

Preparation 266

Compound (266) was obtained in a manner similar to Preparation 22.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.75-2.00 (17H, m), 1.41 (9x1/4H, s), 1.46 (9x3/4H, s), 2.63 (1H, m), 2.93 (1H, dd, J=13.5 and 9.5Hz), 3.06 (1H, dd, J=13.5 and 6Hz), 3.50 (1x3/4H, m), 3.60 (1x1/4H, m), 4.04 (1x1/4H, m), 4.19 (1x3/4H, m), 4.36 (1H, dd, J=8 and 4Hz), 4.75 (1H br), 4.94 (1H, ddd, J=9.5, 7 and 6Hz), 5.10 (1H, d, J=12.5Hz), 5.19 (1H, d, J=12.5Hz), 6.82 (1x3/4H, br-d, J=7Hz), 7.04 (1x1/4H, br-d, J=7Hz), 7.14-7.41 (10H, m);

MASS (ES-): m/e 604.

Preparation 267

Compound (267) was obtained in a manner similar to Preparation 23.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.68-2.32 (17H, m), 2.80 (1/2H, m), 2.95-3.16 (2H, m), 3.50-3.80 (1+1/2H, m), 4.26-4.46 (1+1/2H, m), 4.62 (1/2H, m), 4.86 (1/2H, m), 5.10-5.24 (2H, m), 5.36 (1/2H, m), 7.12-7.40 (10H, m), 8.16 (1H, br), 8.36-8.54 (1+1/2H, m), 8.75 (1/2H, br);

MASS (ES+): m/e 506.

Preparation 268

Compound (268) was obtained in a manner similar to Preparation 24.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.69-2.06 (23H, m), 1.42 (9x1/7H, s), 1.43 (9x6/7H, s), 2.72 (1H, m), 2.92-3.08 (2H, m), 3.57 (1H, m), 4.12 (1H, m), 4.25-4.40 (3H, m), 4.52 (1H, m), 4.93 (1H, m), 5.10 (1H, d, J=12.5Hz), 5.17 (1H, d, J=12.5Hz), 5.20 (1H, br), 6.39 (1x1/7H, d, J=8.5Hz), 6.58 (1x6/7H, d, J=8.5Hz), 6.86 (1H, br-d, J=7Hz), 7.15-7.39 (10H, m), 7.43 (2x1H, dd, J=7.5 and 7.5Hz), 7.55 (1H, m), 8.03 (2x1H, d, J=7.5 and 1.5Hz);

MASS (ES-): m/e 837.

Preparation 269

Compound (269) was obtained in a manner similar to Preparation 17.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.64-2.12 (23H, m), 1.45 (3x3H, s), 2.67 (1H, m), 2.95-3.11 (2H, m), 3.71 (1H, m), 4.08 (1H, m), 4.26-4.64 (4H, m), 4.74 (1H, m), 5.89 (1H, br), 6.95 (1H, br), 7.13-7.34 (5H, m), 7.43 (2x1H, dd, J=7.5 and 7.5Hz), 7.56 (1H, dd, J=7.5 and 7.5Hz), 7.73 (1H, br), 8.04 (2x1H, d, J=7.5Hz);

MASS (ES-): m/e 747.

Preparation 270

Compound (270) was obtained in a manner similar to Preparation 57.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.70-0.90 (2H, m), 1.94-1.30 (6H, m), 1.36-1.67 (7H, m), 1.70-2.18 (8H, m), 2.87-3.01 (2H, m), 3.11 (1H, m), 3.72 (1H, m), 3.96 (1H, m), 4.10 (1H, m), 4.33 (2H, t, J=6Hz), 4.48-4.62 (2H, m), 7.18-7.34 (5H, m), 7.44 (2x1H, dd, J=7.5 and 7.5Hz), 7.55 (1H, dd, J=7.5 and 7.5Hz), 7.90 (1H, d, J=8Hz), 8.04 (2x1H, d, J=7.5Hz), 8.34 (2H, br), 9.07 (1H, d, J=7Hz);

MASS (ES+): m/e 649.

Preparation 271

Compound (271) was obtained in a manner similar to Preparation 76.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.91 (2H, m), 1.06-1.34 (5H, m), 1.36-1.99 (14H, m), 2.18 (1H, m), 2.31 (1H, m), 2.94 (1H, dd, J=13 and 5Hz), 3.10 (1H, m), 3.22 (1H, dd, J=13 and 10Hz), 3.93 (1H, m), 4.31 (1H, t, J=6.5Hz), 4.31 (1H, m), 4.52 (1H, dt, J=10 and 7.5Hz), 4.62 (1H, m), 5.09 (1H, ddd, J=10, 10 and 5Hz), 6.06 (1H, d, J=10Hz), 6.49 (1H, d, J=10Hz), 7.15-7.32 (6H, m), 7.40-7.47 (2H, m), 7.52-7.59 (1H, m), 8.00-8.06 (2H, m);

MASS (ES-) m/e 629.

Preparation 272

Compound (272) was obtained in a manner similar to Preparation 77.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.92 (2H, m), 1.08-1.92 (19H, m), 2.18 (1H, m), 2.31 (1H, m), 2.94 (1H, dd, J=13.5 and 5.5Hz), 3.10 (1H, m), 3.22 (1H, dd, J=13.5 and 10Hz), 3.66 (1H, dt, J=6 and 5Hz), 3.94 (1H, m), 4.29 (1H, dt, J=10 and 7Hz), 4.52 (1H, dt, J=10 and 7.5Hz), 4.63 (1H, m), 5.09 (1H, ddd, J=10, 10 and 5.5Hz), 6.15 (1H, d, J=10Hz), 6.51 (1H, d, J=10Hz), 7.14-7.33 (6H, m);

MASS (ES-): m/e 525.

Preparation 273

Compound (273) was obtained in a manner similar to Preparation 78. The obtained compound was used in Examples 123, 126 and 129.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.90 (2H, m), 1.10-1.32 (4H, m), 1.37-1.95 (13H, m), 2.11-2.55 (4H, m), 2.94 (1H, dd, J=13 and 5Hz), 3.09 (1H, m), 3.21 (1H, dd, J=13 and 10Hz), 3.94 (1H, m), 4.31 (1H, m), 4.52 (1H, dt, J=10 and 7Hz), 4.63 (1H, m), 5.08 (1H, ddd, J=10, 10 and 5Hz), 6.13 (0.6H, d, J=10Hz), 6.32 (0.4H, d, J=10Hz), 6.50 (0.6H, d, J=10Hz), 6.61 (0.4H, d, J=10Hz), 7.17-7.34 (6H, m), 9.76 (1H, t);

MASS (ES+): m/e 525.

Preparation 274

Compound (274) was obtained in a manner similar to Preparation 14.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.44 (9x1/5H, s), 1.46 (9x4/5H, s), 1.78-2.24 (6H, m), 2.69 (2H, t, J=8Hz), 3.31 (1x4/5H, m), 3.60

(1x1/5H, m), 3.70 (1x4/5H, m), 4.25 (1x1/5H, m), 4.42 (1x4/5H, dd, J=8, 3Hz), 4.54 (1x4/5H, m), 4.70 (1x1/5H, m), 4.93 (1x1/5H, m), 5.00 (1x1/5H, d, J=12.5Hz), 5.07 (1x1/5H, d, J=12.5Hz), 5.12 (1x4/5H, d, J=12.5Hz), 5.20 (1x4/5H, d, J=12.5Hz), 5.40 (1H, br-d, J=8Hz), 7.10-7.41 (10H, m);

MASS (ES+): m/e 467.

Preparation 275

Compound (275) was obtained in a manner similar to Preparation 21.

^{1}H-NMR (300MHz, DMSO-d_6, δ): 1.80-2.10 (6H, m), 2.70 (2H, m), 3.40 (1H, m), 3.65 (1H, m), 4.25 (1H, m), 4.35 (1H, m), 5.10 (1H, d, J=12Hz), 5.19 (1H, d, J=12Hz), 7.05-7.44 (10H, m), 8.42 (2H, br-s);

MASS (ES+): m/e 367.

Preparation 276

Compound (276) was obtained in a manner similar to Preparation 22.

^{1}H-NMR (300MHz, DMSO-d_6, δ): 0.71 (3H, t, J=7.3Hz), 1.28 (3x1/4H, s), 1.29 (3x3/4H, s), 1.34 (9x1/4H, s), 1.36 (9x3/4H, s), 1.70-2.62 (10H, m), 3.24-3.44 (3H, m), 3.58 (1H, m), 4.30 (1H, dd, J=9 and 3.5Hz), 4.60 (1H, m), 5.04 (1H, d, J=13Hz), 5.10 (1H, d, J=13Hz), 6.63 (1x1/4H, br-s), 6.80 (1x3/4H, br-s), 7.05-7.41 (10H, m), 7.58 (1x3/4H, d, J=9Hz), 7.92 (1x1/4H, d, J=9Hz);

MASS (ES+): m/e 566.

Preparation 277

Compound (277) was obtained in a manner similar to Preparation 23.

^{1}H-NMR (300MHz, DMSO-d_6, δ): 0.80 (3H, t, J=7Hz), 1.52 (3x1/5H, s), 1.54 (3x4/5H, s), 1.66-2.75 (8H, m), 3.39 (1H, m), 3.60 (1H, m), 4.33 (1H, dd, J=9 and 3Hz), 4.63 (1H, m), 5.00 (1x4/5H, d, J=13Hz), 5.06 (1x1/5H, dd, J=13Hz), 5.12 (1x1/5H, d, J=13Hz), 5.16 (1x4/5H, d, J=13Hz), 7.08 (1H, br-d, J=7Hz), 7.16-7.42 (9H, m), 8.16 (2x4/5H, br-s), 8.20 (2x1/5H, br-s), 8.57 (1x4/5H, d, J=8.5Hz), 8.74 (1x1/5H, d, J=8.5Hz);

MASS (ES+): m/e 466.

Preparation 278

Compound (278) was obtained in a manner similar to Preparation 24.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.76 (3H, t, J=7Hz), 1.43 (3x3H, s), 1.45-2.58 (14H, m), 1.53 (3H, s), 2.65 (2H, t, J=8Hz), 3.32 (1H, m), 3.68 (1H, m), 4.08 (1H, m), 4.31 (2H, t, J=6Hz), 4.44 (1H, dd, J=8 and 2.5Hz), 4.82 (1H, m), 5.12 (1H, m), 5.13 (2H, s), 6.78 (1H, br-d, J=8Hz), 7.01 (1H, s), 7.09-7.38 (10H, m), 7.39-7.47 (2H, m), 7.55 (1H, m), 8.00-8.06 (2H, m);
MASS (ES+): m/e 799.

Preparation 279

Compound (279) was obtained in a manner similar to Preparation 17.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.86 (3H, t, J=7.5Hz), 1.42 (3x3H, s), 1.44-2.30 (14H, m), 1.46 (3H, s), 2.66 (2H, t, J=7Hz), 3.26 (1H, m), 3.74 (1H, m), 4.02 (1H, m), 4.32 (2H, br-t, J=6Hz), 4.42 (1H, m), 4.77 (1H, m), 6.89 (1H, s), 7.11-7.31 (7H, m), 7.43 (2x1H, dd, J=7.5 and 7.5Hz), 7.55 (1H, m), 8.03 (2x1H, dd, J=7.5 and 1.5Hz);
MASS (ES-): m/e 707.

Preparation 280

Compound (280) was obtained in a manner similar to Preparation 18.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.86 (3H, t, J=7.5Hz), 1.37 (3H, s), 1.58 (2H, m), 1.72-2.24 (12H, m), 2.60 (1H, m), 2.72 (1H, m), 3.19 (1H, m), 3.63 (1H, m), 4.09 (1H, m), 4.23-4.38 (3H, m), 4.61 (1H, m), 7.12-7.32 (6H, m), 7.42 (2x1H, dd, J=7.5 and 7.5Hz), 7.56 (1H, m), 7.60 (1H, br-d, J=9Hz), 7.78 (2H, br), 8.01 (2x1H, d, J=7.5Hz);
MASS (ES+): m/e 609.

Preparation 281

Compound (281) was obtained in a manner similar to Preparation 76.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.85 (3H, t, J=7Hz), 1.28 (3H, s), 1.45 (2H, m), 1.61-1.97 (6H, m), 1.98-2.43 (6H, m), 2.64 (2H, m), 3.32 (1H, m), 3.75 (1H, m), 4.24 (1H, dt, J=10 and 7.5Hz), 4.31 (1H, t, J=6.5Hz), 4.72 (1H, m), 4.84 (1H, dt, J=10 and 7.5Hz), 5.81 (1H, s), 7.11 (1H, d, J=10Hz), 7.14-7.23 (3H, m), 7.24-7.32 (2H, m), 7.38-7.48 (3H, m), 7.52-7.60 (2H, m), 8.00-8.06 (2H, m);
MASS (ES-): m/e 589.

Preparation 282

Compound (282) was obtained in a manner similar to Preparation 77.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.87 (3H, t, J=7Hz), 1.28 (3H, s), 1.30-1.70 (5H, m), 1.75-1.92 (3H, m), 2.00-2.42 (6H, m), 2.64 (2H, m), 3.32 (1H, m), 3.65 (2H, br-t, J=6Hz), 3.74 (1H, m), 4.22 (1H, dt, J=10 and 7.5Hz), 4.72 (1H, m), 4.84 (1H, dt, J=10 and 7.5Hz), 5.91 (1H, s), 7.10 (1H, d, J=10Hz), 7.14-7.23 (3H, m), 7.24-7.33 (2H, m), 7.41 (1H, d, J=10Hz);

MASS (ES-): m/e 485.

Preparation 283

Compound (283) was obtained in a manner similar to Preparation 78. The obtained compound was used in Examples 132 and 135.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.87 (3H, t, J=7.5Hz), 1.29 (3H, s), 1.58-1.73 (2H, m), 1.76-1.91 (3H, m), 1.98-2.24 (5H, m), 2.26-2.42 (3H, m), 2.50 (2H, m), 2.64 (2H, m), 3.32 (1H, m), 3.75 (1H, m), 4.23 (1H, m), 4.72 (1H, m), 4.84 (1H, ddd, J=10, 8 and 7Hz), 5.85 (1H, s), 7.12 (1H, d, J=10.5Hz), 7.14-7.32 (5H, m), 7.36 (1H, d, J=10Hz), 9.77 (1H, t, J=1Hz);

MASS (ES-): m/e 483.

Preparation 284

Compound (284) was obtained in a manner similar to Preparation 14.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.49 (9H, s), 1.51-1.63 (1H, m), 1.74-2.01 (3H, m), 2.62-2.80 (1H, m), 2.90 (1H, dd, J=12.5 and 9.6Hz), 3.01 (1H, dd, J=12.5 and 5.6Hz), 3.48-3.66 (1H, m), 4.27 (1H, t, J=7.0Hz), 4.35 (1H, dd, J=8.0 and 3.7Hz), 4.55 (2H, d, J=7.0Hz), 4.56-4.67 (1H, m), 5.11 (1H, d, J=12.4Hz), 5.21 (1H, d, J=12.4Hz), 5.37 (1H, d, J=8.5Hz), 6.62 (1H, br.s), 7.07-7.49 (13H, m), 7.62 (2H, d, J=7.3Hz), 7.79 (2H, d, J=7.8Hz);

MASS (ES+): m/e 690.49 (M+1).

Preparation 285

Compound (285) was obtained in a manner similar to Preparation 15.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.80 (3H, t, J=7.3Hz), 1.39 (1.5H, s), 1.40 (1.5H, s), 1.43 (9H, s), 1.49-1.65 (2H, m), 1.71-2.07 (4H, m), 2.69-2.85 (1H, m), 2.91 (1H, dd, J=12.9 and 9.2Hz), 3.01 (1H,

dd, J=12.9 and 5.4Hz), 3.49-3.62 (1H, m), 4.27 (1H, t, J=6.6Hz), 4.37 (1H, dd, J=7.8 and 3.4Hz), 4.54 (2H, t, J=6.6Hz), 4.85-4.98 (1H, m), 5.01-5.20 (3H, m), 6.52-6.67 (1H, m), 6.84 (1H, d, J=8.1Hz), 7.10-7.19 (2H, m), 7.20-7.38 (9H, m), 7.42 (2H, t, J=7.3Hz), 7.61 (2H, t, J=7.4Hz), 7.79 (2H, t, J=7.4Hz);
MASS (ES+): m/e 789.65 (M+1).

Preparation 286

Compound (286) was obtained in a manner similar to Preparation 16.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.72 (3H, t, J=7.3Hz), 1.43 (3H, s), 1.44 (9H, s), 1.45-1.98 (9H, m), 2.15-2.36 (1H, m), 2.74-3.03 (3H, m), 3.52-3.66 (1H, m), 4.20-4.34 (3H, m), 4.39 (1H, dd, J=7.8 and 3.5Hz), 4.52 (2H, t, J=6.6Hz), 4.85-4.99 (1H, m), 5.01-5.21 (3H, m), 6.61-6.84 (2H, m), 6.98 (1H, s), 7.11 (2H, d, J=8.4Hz), 7.20-7.36 (1H, m), 7.41 (2H, t, J=7.7Hz), 7.50-7.58 (1H, m), 7.61 (2H, d, J=7.3Hz), 7.78 (2H, d, J=7.3Hz), 8.03 (2H, d, J=6.9Hz).

Preparation 287

Compound (287) was obtained in a manner similar to Preparation 17.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.76 (3H, t, J=7.3Hz), 1.37-3.01 (15H, m), 1.44 (12H, s), 3.61-3.75 (1H, m), 3.94-4.08 (1H, m), 4.22-4.40 (4H, m), 4.54 (2H, br-d, J=6.6Hz), 4.83-4.98 (1H, m), 5.24 (1H, br.s), 6.60 (0.4H, br-d, J=8.4Hz), 6.67 (1H, br.s), 6.84 (1H, br.s), 6.98 (0.6H, br-d, J=8.1Hz), 7.14 (2H, br-d, J=8.1Hz), 7.21-7.47 (6H, m), 7.48-7.66 (3H, m), 7.71-7.82 (2H, m), 7.99-8.08 (2H, m);
MASS (ES+): m/e 932.42 (M+1).

Preparation 288

Compound (288) was obtained in a manner similar to Preparation 18.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.71 (3H, br.s), 1.38 (3H, br.s), 1.47-2.22 (12H, m), 2.74-3.19 (3H, m), 3.56-3.81 (1H, m), 4.08-4.51 (6H, m), 4.82-5.04 (1H, m), 7.02-7.16 (2H, m), 7.17-7.43 (9H, m), 7.44-7.67 (4H, m), 7.69-7.81 (2H, m), 7.91-8.05 (2H, m), 8.11-8.35 (2H, m), 8.37-8.62 (1H, m);
MASS (ES+): m/e 832.64 (M+1).

Preparation 289

Compound (289) was obtained in a manner similar to Preparation 76.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.82 (3H, t, J=7.3Hz), 1.27 (3H, s), 1.35-2.02 (8H, m), 2.06-2.24 (2H, m), 2.25-2.41 (2H, m), 2.91 (1H, dd, J=13.6 and 6.2Hz), 3.08-3.32 (2H, m), 3.79-3.92 (1H, m), 4.18-4.30 (2H, m), 4.31 (2H, t, J=6.3Hz), 4.54 (2H, d, J=6.6Hz), 4.66 (1H, br-d, J=7.0Hz), 5.14 (1H, dt, J=10.2 and 6.3Hz), 5.90 (1H, s), 6.63 (1H, br.s), 7.13 (1H, d, J=10.6Hz), 7.16 (2H, d, J=8.8Hz), 7.23-7.37 (4H, m), 7.38-7.48 (4H, m), 7.51-7.65 (4H, m), 7.78 (2H, d, J=7.3Hz), 8.00-8.07 (2H, m);

MASS (ES+): m/e 813.89 (M).

Preparation 290

Compound (290) was obtained in a manner similar to Preparation 21.

^{1}H-NMR (300MHz, DMSO-d_6, δ): 1.52 (1H, m), 1.66-1.86 (2H, m), 1.94 (1H, m), 2.72 (1H, m), 2.97 (1H, dd, J=13.5 and 8.5Hz), 3.14 (1H, dd, J=13.5 and 6Hz), 3.56 (1H, m), 4.28 (1H, dd, J=9 and 3.5Hz), 4.41 (1H, br-dd, J=8.5 and 6Hz), 5.08 (1H, d, J=12.5Hz), 5.19 (1H, d, J=12.5Hz), 7.20-7.43 (10H, m), 8.40 (2H, br-s);

MASS (ES+): m/e 353.

Preparation 291

Compound (291) was obtained in a manner similar to Preparation 22.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.40 (3x3H, s), 1.47 (1H, m), 1.58-1.94 (3H, m), 2.56 (1H, m), 2.77 (1H, dd, J=13 and 10Hz), 2.83-3.08 (3H, m), 3.48 (1H, m), 3.76 (3H, s), 4.32 (1H, dd, J=8 and 4Hz), 4.84-5.02 (2H, m), 5.10 (1H, d, J=12.5Hz), 5.17 (1H, d, J=12.5Hz), 6.67 (1H, d, J=8Hz), 6.83 (2x1H, d, J=8Hz), 6.98-7.40 (11H, m), 7.09 (2x1H, d, J=8Hz);

MASS (ES+): m/e 630.

Preparation 292

Compound (292) was obtained in a manner similar to Preparation 16.

^{1}H-NMR (300MHz, DMSO-d_6, δ): 1.70-2.30 (4H, m), 2.41-2.98 (4H, m), 3.26-3.76 (2H, m), 3.70 (3x1/5H, s), 3.71 (3x4/5H, s), 3.83-4.01 (2H, m), 4.32 (1x4/5H, dd, J=8 and 3Hz), 4.44 (1x1/5H, m),

4.88 (1x4/5H, m), 5.06 (1x1/5H, m), 5.10 (1x4/5H, d, J=12.5Hz), 5.14 (1x4/5H, d, J=12.5Hz), 5.21 (1x1/5H, d, J=12.5Hz), 5.31 (1x1/5H, d, J=12.5Hz), 6.67-6.78 (4x1/5H, m), 6.84 (2x4/5H, d, J=9Hz), 7.02 (2x4/5H, d, J=9Hz), 7.08-7.44 (10H, m), 8.07 (2H, br), 9.00 (1x4/5H, d, J=8Hz), 9.26 (1x1/5H, d, J=8Hz);
MASS (ES+): m/e 530.

Example 1

To a stirred solution of dimethyl (3R)-tert-butyldimethylsilyloxy-2-oxobutylphosphonate (812 mg) in water and tetrahydrofuran (1:40) (7.5 ml) was added barium hydroxide octahydrate (482 mg) in one portion. The mixture was stirred at ambient temperature for 30 minutes. To the mixture was added a solution of Compound C1-3 (980 mg) in water and tetrahydrofuran (1:40) (1.5 ml once, 1 ml twice), and stirred for 1 hour. 10% Aqueous citric acid solution (50 ml) was added to the mixture to quench the reaction, stirred for 15 minutes under ice-cooling, and extracted with ethyl acetate (300 ml). The organic layer was washed with 10% citric acid (50 ml), water (50 ml) and brine (50 ml), dried over sodium sulfate and evaporated in vacuo. The residue was purified by flash column chromatography (eluted with ethyl acetate/hexane = 2:3 to 1:1 v/v) to give Compound E1 as a white foam (852 mg).

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.83 (3H, s), 1.09 (9H, s), 1.22 (3H, d, J=7.0Hz), 1.28 (3H, s), 1.37-1.51 (2H, m), 1.54-1.89 (4H, m), 2.09-2.37 (6H, m), 2.89 (1H, dd, J=14.0 and 6.2Hz), 3.18 (1H, dd, J=14.0 and 9.9Hz), 3.19-3.29 (1H, m), 3.80-3.91 (1H, m), 4.15-4.28 (1H, m), 4.27 (1H, q, J=7.0Hz), 4.63-4.70 (1H, m), 5.02 (2H, s), 5.06-5.19 (1H, m), 5.84 (1H, s), 6.61 (1H, d, J=15.4Hz), 6.80-6.89 (1H, m), 6.88 (2H, d, J=8.5Hz), 7.10-7.15 (1H, m), 7.14 (2H, d, J=8.5Hz), 7.28-7.49 (11H, m), 7.51 (1H, d, J=10.7Hz), 7.55-7.69 (4H, m);
MASS (ES+): m/e 885.56 (M+).

Example 2

Compound E2 was obtained in a manner similar to Example 1.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.83 (3H, t, J=6.7Hz), 1.09 (9H, s), 1.23 (3H, d, J=6.5Hz), 1.28 (3H, s), 1.35-1.53 (2H, m), 1.62-1.90 (3H, m), 2.09-2.38 (7H, m), 2.89 (1H, dd, J=13.5 and 5.8Hz), 3.18 (1H, dd, J=13.5 and 9.9Hz), 3.21-3.31 (1H, m), 3.81-3.92 (1H, m), 4.15-4.27 (1H, m), 4.27 (1H, q, J=6.5Hz), 4.67 (1H, br. d,

J=5.6Hz), 5.03 (2H, s), 5.08-5.19 (1H, m), 5.79 (1H, s), 6.61 (1H, d, J=15.8Hz), 6.81-6.92 (1H, m), 6.88 (2H, d, J=8.8Hz), 7.09-7.17 (1H, m), 7.14 (2H, d, J=8.8Hz), 7.30-7.46 (11H, m), 7.50 (1H, d, J=10.7Hz), 7.57-7.62 (2H, m), 7.63-7.69 (2H, m);
MASS (ES+): m/e 885.45 (M+).

Example 3

To a solution of the Compound E1 (86.9 ml) in methanol (3 ml), Pd-$BaSO_4$ (56.2 mg) was added and stirred for 1.25 hours under hydrogen atmosphere. The catalyst was filtered through a pad of Celite® and the solvent was evapolated under reduced pressure. The residue was purified by preparative thin layer chromatography to give Compound E3 as an oil (74.7 mg).

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.83 (3H, t, J=7.3Hz), 1.10 (9H, s), 1.26 (3H, d, J=6.6Hz), 1.10-1.36 (6H, m), 1.27 (3H, s), 1.40-1.65 (3H, m), 1.67-1.85 (4H, m), 2.08-2.27 (2H, m), 2.27-2.40 (2H, m), 2.49 (2H, ddd, J=9.2, 7.0 and 1.5Hz), 2.88 (1H, dd, J=13.8 and 5.9Hz), 3.18 (1H, dd, J=13.8 and 9.9Hz), 3.18-3.30 (1H, m), 3.81-3.92 (1H, m), 4.14-4.24 (2H, m), 4.18 (1H, d, J=5.8Hz), 5.02 (2H, s), 5.13 (1H, ddd, J=16.1, 9.9 and 6.2Hz), 5.84 (1H, s), 6.88 (2H, d, J=8.8Hz), 7.07 (1H, d, J=10.3Hz), 7.15 (2H, d, J=8.4Hz), 7.25-7.45 (11H, m), 7.56 (1H, d, J=10.38Hz), 7.55-7.68 (4H, m).

Example 4

To a solution of the Compound E1 in methanol-dioxane mixture (1:1) (20 ml) was added 10% palladium on carbon (300 mg) and the mixture was shaken under an atmosphere of hydrogen (4 atm) at ambient temperature for 20 hours. The mixture was filtered through a pad of Celite® and the filtrate was purified by flash chromatography (eluted with ethyl acetate/hexane = 1:1 to 2:2 v/v) to give Compound E4 as a colorless amorphous compound (610 mg).

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.83 (3H, t, J=7.3Hz), 1.10 (9H, s), 1.14-1.56 (6H, m), 1.19 (3H, d, J=6.8Hz), 1.28 (3H, s), 1.69-1.88 (4H, m), 2.07-2.24 (2H, m), 2.24-2.37 (2H, m), 2.45-2.56 (2H, m), 2.88 (1H, dd, J=13.5 and 6.3Hz), 3.16 (1H, dd, J=13.5 and 9.8Hz), 3.20-3.31 (1H, m), 3.77-3.89 (1H, m), 4.11-4.20 (1H, m), 4.18 (1H, q, J=6.8Hz), 4.67 (1H, br. d, J=6.8Hz), 5.06-5.18 (1H, m), 5.10 (1H, s), 5.89 (1H, s), 6.73 (2H, d, J=8.4Hz), 7.05-7.10 (1H, m), 7.09 (2H, d, J=8.4Hz), 7.32-7.48 (6H, m), 7.53-7.70 (5H, m);
MASS (ES+): m/e 797.55 (M+).

Example 5

Compound E5 was obtained from the Compound E2 in a manner similar to Example 4.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.83 (3H, t, J=7.3Hz), 1.10 (9H, s), 1.19 (3H, d, J=6.7Hz), 1.21-1.61 (7H, m), 1.28 (3H, s), 1.69-1.88 (3H, m), 2.08-2.24 (2H, m), 2.25-2.38 (2H, m), 2.51 (2H, t, J=6.8Hz), 2.89 (1H, dd, J=13.5 and 6.2Hz), 3.16 (1H, dd, J=13.5 and 9.6Hz), 3.21-3.31 (1H, m), 3.77-3.90 (1H, m), 4.08-4.24 (2H, m), 4.67 (1H, br. d, J=5.9Hz), 5.05-5.18 (1H, m), 5.20 (1H, s), 5.85 (1H, s), 7.04-7.10 (1H, m), 7.09 (2H, d, J=8.5Hz), 7.32-7.48 (6H, m), 7.53-7.68 (5H, m);

MASS (ES+): m/e 797.57 (M).

Example 6

To a stirred solution of the Compound E3 (74.7 mg) in tetrahydrofuran (3 ml) was added tetrabutylammonium fluoride (1.0M in tetrahydrofuran, 0.1 ml) at ambient temperature and the mixture was stirred for 40 minutes at the same temperature. The reaction mixture was diluted with water (10 ml) and the organic layer was extracted with ethyl acetate (5 ml, twice). The combined organic phase was washed with brine (5 ml), dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated under reduced pressure and the residue was purified by preparative thin layer chromatography (chloroform : methanol = 10:1 v/v) to give Compound E6 (51.6 mg) as a colorless oil.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.83 (3H, t, J=7.3Hz), 1.20-1.40 (4H, m), 1.28 (3H, s), 1.37 (3H, d, J=7.0Hz), 1.56-1.70 (2H, m), 1.70-1.88 (2H, m), 2.08-2.24 (2H, m), 2.25-2.58 (4H, m), 2.89 (1H, dd, J=13.6 and 5.9Hz), 3.18 (1H, dd, J=13.6 and 9.9Hz), 3.19-3.30 (1H, m), 3.61 (1H, d, J=4.4Hz), 3.80-3.90 (1H, m), 4.15-4.28 (2H, m), 4.68 (6.6H, d), 5.02 (2H, s), 5.15 (1H, ddd, J=16.1, 9.9 and 6.2Hz), 5.89 (1H, s), 6.88 (2H, d, J=8.8Hz), 7.10-7.18 (3H, m), 7.25-7.45 (5H, m), 7.54 (1H, d, J=10.3Hz);

MASS(ES+): m/e 648.35 (M+1).

Example 7

Compound E7 was obtained from the Compound E5 in a manner similar to Example 6.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (3H, t, J=6.9Hz), 1.22-1.69 (7H, m), 1.28 (3H, s), 1.38 (3H, d, J=7.1Hz), 1.70-1.88 (3H, m), 2.07-2.24 (2H, m), 2.24-2.36 (2H, m), 2.88 (1H, dd, J=13.4 and 5.5Hz),

3.15 (1H, dd, J=13.4 and 9.4Hz), 3.20-3.32 (1H, m), 3.57 (1H, d, J=4.6Hz), 3.77-3.89 (1H, m), 4.13-4.28 (2H, m), 4.68 (1H, br. d, J=5.8Hz), 5.05-5.18 (1H, m), 5.40 (1H, s), 5.89 (1H, s), 6.73 (2H, d, J=8.0Hz), 7.09 (2H, d, J=8.0Hz), 7.12 (1H, d, J=10.0Hz), 7.55 (1H, d, J=10.2Hz);

MASS (ES+): m/e 559.41 (M+1).

Example 8

Compound E8 was obtained from the Compound E4 in a manner similar to Example 6.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (3H, t, J=7.1Hz), 1.21-1.41 (4H, m), 1.29 (3H, s), 1.38 (3H, d, J=7.0Hz), 1.53-1.69 (3H, m), 1.70-1.89 (3H, m), 2.06-2.23 (2H, m), 2.24-2.38 (2H, m), 2.39-2.55 (2H, m), 2.88 (1H, dd, J=13.5 and 5.8Hz), 3.15 (1H, dd, J=13.5 and 9.6Hz), 3.19-3.31 (1H, m), 3.57 (1H, d, J=4.7Hz), 3.77-3.89 (1H, m), 4.07-4.29 (2H, m), 4.67 (1H, br d, J=6.5Hz), 5.06-5.18 (1H, m), 5.29 (1H, s), 15.93 (1H, s), 6.73 (2H, d, J=8.5Hz), 7.09 (2H, d, J=8.5Hz), 7.12 (1H, d, J=10.0Hz), 7.55 (1H, d, J=10.3Hz);

MASS (ES+): m/e 559.31 (M+1).

Example 9

Compound E9 was obtained from the Compound (81) in a manner similar to Example 1.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (3H, t, J=7.3Hz), 1.09 (3x3H, s), 1.22 (3H, d, J=7Hz), 1.28 (3H, s), 1.38-1.52 (2H, m), 1.56-1.90 (4H, m), 2.08-2.40 (6H, m), 2.89 (1H, dd, J=14 and 6Hz), 3.18 (1H, dd, J=14 and 10Hz), 3.26 (1H, m), 3.77 (3H, s), 3.86 (1H, m), 4.21 (1H, m), 4.26 (1H, q, J=7Hz), 4.66 (1H, m), 5.14 (1H, ddd, J=10, 10 and 6Hz), 5.84 (1H, s), 6.62 (1H, br-d, J=16Hz), 6.81 (2x1H, d, J=8.5Hz), 6.84 (1H, dt, J=16 and 7Hz), 7.14 (2x1H, d, J=8.5Hz), 7.29-7.45 (6H, m), 7.51 (1H, d, J=10Hz), 7.55-7.68 (4H, m);

MASS (ES-): m/e 807.

Example 10

Compound E10 was obtained from the Compound (80) in a manner similar to Example 2.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.83 (3H, t, J=7.8Hz), 1.21 (9H, s), 1.26 (3H, d, J=6.9Hz), 1.63 (3H, s), 1.70-1.58 (4H, m), 1.71-1.79 (3H, m), 2.09-2.39 (6H, m), 2.89 (1H, dd, J=13.8 and 5.7Hz), 3.18 (1H, dd, J=13.8 and 9.6Hz), 3.22-3.31 (1H, m), 3.77 (3H, s), 3.79-3.92 (1H, m), 4.18-4.27 (1H, m), 4.27 (1H, q, J=6.9Hz), 5.13

(1H, ddd, J=9.9, 9.9 and 5.7Hz), 5.84 (1H, s), 6.61 (1H, d, J=15.3Hz), 6.81 (2H, d, J=8.7Hz), 6.86 (1H, dt, J=15.3 and 6.9Hz), 7.15 (2H, d, J=8.7Hz), 7.31-7.48 (5H, m), 7.51 (1H, d, J=10.5Hz), 7.57-7.69 (5H, m);

MASS (ES+): m/e 809.48 (M).

Example 11

Compound E11 was obtained from the Compound E9 in a manner similar to Example 3.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (3H, t, J=7.3Hz), 1.10 (3x3H, s), 1.18 (3H, d, J=7Hz), 1.20-1.30 (4H, m), 1.28 (3H, s), 1.40-1.51 (2H, m), 1.60 (1H, m), 1.68-1.88 (3H, m), 2.09-2.24 (2H, m), 2.25-2.38 (2H, m), 2.51 (2H, m), 2.89 (1H, dd, J=13.5 and 6Hz), 3.18 (1H, dd, J=13.5 and 10Hz), 3.26 (1H, m), 3.85 (1H, m), 4.18 (1H, m), 4.18 (1H, q, J=7Hz), 4.67 (1H, m), 5.13 (1H, ddd, J=10, 10 and 6Hz), 5.85 (1H, s), 6.81 (2x1H, d, J=8.5Hz), 7.08 (1H, d, J=10Hz), 7.14 (2x1H, d, J=8.5Hz), 7.33-7.48 (6H, m), 7.56 (1H, d, J=10Hz), 7.59-7.68 (4H, m);

MASS (ES+): m/e 811.

Example 12

Compound E12 was obtained from the Compound E10 in a manner similar to Example 3.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (3H, t, J=7.5Hz), 1.10 (9H, s), 1.16-1.32 (11H, m), 1.18 (3H, d, J=6.6Hz), 1.38-1.51 (1H, m), 1.61 (3H, s), 1.68-1.88 (2H, m), 2.08-2.24 (2H, m), 2.25-2.39 (2H, m), 2.50 (2H, t), 2.89 (1H, dd, J=13.5 and 6.0Hz), 3.18 (1H, dd, J=13.5 and 9.9Hz), 3.23-3.30 (1H, m), 3.77 (3H, s), 3.81-3.90 (1H, m), 4.13-4.23 (1H, m), 4.18 (1H, q, J=6.6Hz), 4.64-4.69 (1H, m), 5.13 (1H, ddd, J=9.9, 9.9 and 6.3Hz), 5.84 (1H, s), 6.81 (2H, d, J=8.7Hz), 7.08 (1H, d, J=9.9Hz), 7.15 (2H, d, J=8.7Hz), 7.33-7.48 (6H, m), 7.55 (1H, d, J=10.2Hz);

MASS (ES+): m/e 811.49.

Example 13

Compound E13 was obtained from the Compound E11 in a manner similar to Example 6.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (3H, t, J=7.3Hz), 1.20-1.40 (4H, m), 1.29 (3H, s), 1.38 (3H, d, J=7Hz), 1.54-1.69 (3H, m), 1.70-1.90 (3H, m), 2.08-2.23 (2H, m), 2.26-2.56 (4H, m), 2.89 (1H, dd, J=14 and 6Hz), 3.18 (1H, dd, J=14 and 10Hz), 3.26 (1H, m), 3.56 (1H, d, J=5Hz), 3.86 (1H, m), 4.14-4.30 (2H, m), 4.67 (1H, m),

5.13 (1H, ddd, J=10, 10 and 6Hz), 5.87 (1H, s), 6.81 (2x1H, d, J=9Hz), 7.12 (1H, d, J=11Hz), 7.14 (2x1H, d, J=9Hz), 7.53 (1H, d, J=10Hz);
MASS (ES-): m/e 571;
$[\alpha]_D^{25}$ = -116.5° (c=0.31, $CHCl_3$).

Example 14

Compound E14 was obtained from the Compound E12 in a manner similar to Example 6.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.83 (3H, t, J=6.9Hz), 1.23-1.40 (2H, m), 1.38 (3H, d, J=7.2Hz), 1.55-1.90 (6H, m), 1.64 (3H, s), 2.05-2.58 (6H, m), 2.88 (1H, dd, J=13.5 and 6.0Hz), 3.18 (1H, dd, J=13.5 and 9.9Hz), 3.21-3.30 (1H, m), 3.55 (1H, d, J=4.8Hz), 3.78 (3H, s), 3.80-3.90 (1H, m), 4.16-4.28 (1H, m), 4.19 (1H, q, 7.2Hz), 4.64-4.70 (1H, m), 5.13 (1H, ddd, J=9.9, 9.9 and 6.0Hz), 5.89 (1H, s), 6.81 (2H, d, J=8.4Hz), 7.12 (1H, d, J=9.3Hz), 7.14 (2H, d, J=8.4Hz), 7.53 (1H, d, J=10.2Hz);
MASS (ES+): m/e 573.49 (M+1).

Example 15

Compound E15 was obtained from the Compound (84) in a manner similar to Example 1.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.83 (3H, t, J=7.0Hz), 1.10 (9H s), 1.23 (3H, d, J=6.9Hz), 1.29 (3H, s), 1.36-1.55 (2H, m), 1.63-1.90 (4H, m), 2.07-2.39 (6H, m), 2.95 (1H, dd, J=13.9 and 7.4Hz), 3.21 (1H, dd, J=13.9 and 8.7Hz), 3.22-3.34 (1H, m), 3.80-3.91 (1H, m), 4.18-4.29 (1H, m), 4.28 (1H, q, J=6.9Hz), 4.68 (1H, br. d, J=7.1Hz), 5.08-5.20 (1H, m), 5.83 (1H, s), 6.62 (1H, d, J=15.7Hz), 6.82-6.98 (1H, m), 6.97 (2H, t, J=8.7Hz), 7.09 (1H, d, J=10.6Hz), 7.20 (2H, dd, J=8.7 and 5.4Hz), 7.29-7.48 (6H, m), 7.55 (1H, d, J=10.6Hz), 7.56-7.69 (4H, m);
MASS (ES+): m/e 797.59 (M+1).

Example 16

Compound E16 was obtained from the Compound E15 in a manner similar to Example 3 except that 10% palladium on carbon was used instead of Pd-$BaSO_4$.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.83 (3H, t, J=7.3Hz), 1.10 (9H, s), 1.16-1.32 (3H, m), 1.18 (3H, d, J=6.7Hz), 1.28 (3H, s), 1.38-1.62 (4H, m), 1.72-1.88 (3H, m), 2.09-2.38 (4H, m), 2.46-2.55 (2H, m), 2.93 (1H, dd, J=13.2 and 7.1Hz), 3.20 (1H, dd, J=13.2 and 8.7Hz), 3.22-3.32 (1H, m), 3.79-3.89 (1H, m), 4.12-4.24 (1H, m), 4.19 (1H,

q, J=6.7Hz), 4.67 (1H, br. d, J=5.4Hz), 5.08-5.19 (1H, m), 5.83 (1H, s), 6.96 (2H, t, J=8.6Hz), 7.04 (1H, d, J=10.2Hz), 7.19 (2H, dd, J=8.6 and 5.5Hz), 7.32-7.48 (6H, m), 7.54-7.67 (5H, m);
MASS (ES+): m/e 799.52 (M).

Example 17

Compound E17 was obtained from the Compound E16 in a manner similar to Example 6.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.83 (3H, t, J=7.3Hz), 1.24-1.39 (6H, m), 1.28 (3H, s), 1.38 (3H, d, J=7.2Hz), 1.54-1.69 (1H, m), 1.71-1.89 (3H, m), 2.08-2.58 (6H, m), 2.93 (1H, dd, J=13.9 and 6.3Hz), 3.20 (1H, dd, J=13.9 and 9.6Hz), 3.21-3.32 (1H, m), 3.55 (1H, d, J=4.7Hz), 3.78-3.91 (1H, m), 4.14-4.29 (2H, m), 4.68 (1H, br. d, J=5.8Hz), 5.08-5.19 (1H, m), 5.87 (1H, s), 6.96 (2H, t, J=8.8Hz), 7.07 (1H, d, J=10.4Hz), 7.19 (2H, dd, J=8.8 and 5.5Hz), 7.56 (1H, d, J=10.7Hz);
MASS (ES+): m/e 561.46 (M+1).

Example 18

Compound E18 was obtained from the Compound (87) in a manner similar to Example 1.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.09 (9H, s), 1.22 (1H, d, J=7.2Hz), 1.37-1.88 (15H, m), 2.12-2.38 (3H, m), 2.43-2.58 (2H, m), 2.95 (1H, dd, J=13.5 and 6.0Hz), 3.25 (1H, dd, J=13.5 and 10.2Hz), 3.28-3.13 (1H, m), 3.85-3.95 (1H, m), 4.22 (1H, dt, J=10.2 and 7.8Hz), 4.27 (1H, q, J=7.2Hz), 4.64-4.69 (1H, m), 5.15 (1H, ddd, J=9.9, 9.9 and 5.7Hz), 6.16 (1H, s), 6.61 (1H, d, J=15.6Hz), 6.87 (1H, dt, J=15.6 and 6.9Hz), 7.16-7.33 (5H, m), 7.33-7.48 (8H, m), 7.57-7.74 (4H, m);
MASS (ES+): m/e 791.60 (M).

Example 19

Compound E19 was obtained from the Compound E18 in a manner similar to Example 3 except that 10% palladium on carbon was used instead of Pd-$BaSO_4$.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.10 (9H, s), 1.01-1.84 (17H, m), 1.18 (3H, d, J=6.9Hz), 2.11-2.36 (2H, m), 2.41-2.58 (3H, m), 2.95 (1H, dd, J=10.5 and 6.0Hz), 3.15-3.26 (1H, m), 3.26 (1H, dd, J=10.5 and 13.5Hz), 3.84-3.94 (1H, m), 4.12 (1H, dt, J=6.9 and 7.5Hz), 4.18 (1H, q, J=6.9Hz), 4.63-4.69 (1H, m), 5.14 (1H, ddd, J=9.6, 9.6 and 6.0Hz), 6.14 (1H, s), 7.13 (1H, d, J=10.2Hz), 7.17-7.31 (4H, m), 7.32-7.49 (8H, m), 7.57-7.66 (4H, m);

MASS (ES+): m/e 793.57 (M).

Example 20

Compound E20 was obtained from the Compound E19 in a manner similar to Example 6.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.19-1.87 (17H, m), 1.38 (3H, d, J=7.2Hz), 2.11-2.23 (1H, m), 2.24-2.39 (2H, m), 2.40-2.58 (2H, m), 2.95 (1H, dd, J=13.5 and 6.0Hz), 3.15-3.25 (1H, m), 3.25 (1H, dd, J=13.5 and 10.2Hz), 3.56 (1H, d, J=4.8Hz), 3.86-3.95 (1H, m), 4.12 (1H, q, J=7.2Hz), 4.28-4.12 (1H, m), 4.63-4.69 (1H, m), 5.15 (1H, ddd, J=10.2, 10.2 and 6.0Hz), 6.18 (1H, s), 7.14-7.34 (6H, m), 7.43 (1H, d, J=10.2Hz);

MASS (ES+): m/e 555.41 (M+1).

Example 21

Compound 21 was obtained from the Compound (90) in a manner similar to Example 1.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.812 (3H, t, J=7.2Hz), 1.10 (6H, s), 1.11 (3H, s), 1.27 (3H, s), 1.37-1.91 (8H, m), 2.08-2.39 (6H, m), 3.06 (1H, dd, J=14.7 and 6.9Hz), 3.25-3.36 (1H, m), 3.27 (1H, dd, J=14.7 and 8.7Hz), 3.80-3.89 (1H, m), 4.18-4.31 (1H, m), 4.26 (2H, t, J=6.6Hz), 4.66-4.71 (1H, m), 5.13-5.23 (1H, m), 5.89 (1H, s), 6.62 (1H, d, J=15.9Hz), 6.87 (1H, dt, J=15.9 and 6.9Hz), 7.01 (1H, d, J=10.8Hz), 7.30-7.49 (7H, m), 7.56-7.68 (8H, m);

MASS (ES+): m/e 804.62 (M+1).

Example 22

Compound E22 was obtained from the Compound E21 in a manner similar to Example 3 except that 10% palladium on carbon was used instead of 5% Pd-$BaSO_4$.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.807 (3H, t, J=6.9Hz), 1.10 (9H, s), 1.28 (3H, s), 1.38-1.90 (11H, m), 2.06-2.39 (6H, m), 2.51 (2H, dt, J=7.2 and 2.7Hz), 3.06 (1H, dd, J=13.5 and 7.5Hz), 3.26-3.36 (1H, m), 3.27 (1H, dd, J=13.5 and 9.0Hz), 3.79-3.88 (1H, m), 4.19 (1H, dq, J=6.6 and 2.7Hz), 4.25 (1H, dt, J=13.8 and 6.9Hz), 4.66-4.71 (1H, m), 5.18 (1H, dt, J=9.6 and 8.1Hz), 5.87 (1H, s), 6.95 (1H, d, J=10.2Hz), 7.32-7.49 (7H, m), 7.58-7.69 (7H, m), 7.58 (1H, d, J=9.0Hz);

MASS (ES+): m/e 806.38 (M+1).

Example 23

Compound E23 was obtained from the Compound E22 in a manner similar to Example 6.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.811 (3H, t, J=7.5Hz), 1.24-1.68 (11H, m), 1.38 (3H, d, J=7.2Hz), 1.75-1.89 (3H, m), 2.06-2.57 (6H, m), 3.06 (1H, dd, J=14.1 and 7.5Hz), 3.26-3.36 (1H, m), 3.26 (1H, dd, J=14.1 and 8.7Hz), 3.79-3.88 (1H, m), 4.15-4.28 (2H, m), 4.65-4.71 (1H, m), 5.18 (1H, dt, J=8.4 and 7.2Hz), 5.90 (1H, s), 6.99 (1H, d, J=10.5Hz), 7.33-7.39 (2H, m), 7.56-7.61 (2H, m), 7.63 (1H, d, J=10.2Hz);

MASS (ES+): m/e 568.50 (M+1).

Example 24

Compound E24 was obtained from the Compound (93) in a manner similar to Example 1.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (3H, t, J=7.2Hz), 1.09 (5H, s), 1.10 (4H, s), 1.22 (3H, d, J=6.9Hz), 1.28 (3H, s), 1.37-1.90 (8H, m), 1.39 (3H, t, J=6.9Hz), 2.10-2.38 (4H, m), 2.88 (1H, dd, J=13.5 and 5.7Hz), 3.19 (1H, dd, J=13.5 and 9.6Hz), 3.12-3.30 (1H, m), 3.81-3.90 (1H, m), 3.99 (2H, q, J=6.9Hz), 4.16-4.31 (2H, m), 4.64-4.69 (1H, m), 5.13 (1H, dt, J=9.6 and 5.7Hz), 5.85 (1H, s), 6.61 (1H, d, J=15.9Hz), 6.79 (2H, d, J=8.4Hz), 6.86 (1H, dt, J=15.9Hz), 7.12-7.17 (1H, m), 7.13 (2H, d, J=8.4Hz), 7.31-7.47 (5H, m), 7.50 (1H, d, J=10.2Hz), 7.56-7.68 (5H, m);

MASS (ES+): m/e 823.64 (M+1).

Example 25

Compound E25 was obtained from the Compound E24 in a manner similar to Example 16.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.85 (3H, t, J=7.2Hz), 1.11 (9H, s), 1.20 (3H, d, J=6.9Hz), 1.20-1.65 (7H, m), 1.29 (3H, s), 1.40 (3H, t, J=6.9Hz), 1.71-1.86 (3H, m), 2.09-2.24 (2H, m), 2.26-2.38 (2H, m), 2.52 (1H, dt, J=7.5 and 2.1Hz), 2.89 (1H, dd, J=13.5 and 5.7Hz), 3.13-3.31 (1H, m), 3.23 (1H, dd, J=13.5 and 9.6Hz), 3.81-3.90 (1H, m), 4.00 (1H, q, J=6.9Hz), 4.19 (1H, dq, J=6.9 and 2.1Hz), 4.64-4.70 (1H, m), 5.14 (1H, dt, J=9.6 and 5.7Hz), 5.83 (1H, s), 6.80 (2H, d, J=8.7Hz), 7.10 (1H, d, J=11.1Hz), 7.14 (2H, d, J=8.7Hz), 7.34-7.48 (5H, m), 7.55 (1H, d, J=10.5Hz), 7.60-7.67 (5H, m);

MASS (ES+): m/e 825.65 (M+1).

Example 26

Compound E26 was obtained from the Compound E25 in a manner similar to Example 6.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (3H, t, J=6.9Hz), 1.20-1.42 (7H,

m), 1.28 (3H, s), 1.39 (3H, t, J=7.2Hz), 1.52-1.69 (3H, m), 1.71-1.87 (3H, m), 2.08-2.24 (2H, m), 2.26-2.39 (2H, m), 2.46 (2H, dt, J=11.7 and 7.2Hz), 2.88 (1H, dd, J=13.2 and 5.7Hz), 3.17 (1H, dd, J=13.2 and 11.2Hz), 3.22-3.30 (1H, m), 3.55 (1H, d, J=4.5Hz), 3.81-3.90 (1H, m), 3.99 (2H, q, J=7.2Hz), 4.14-4.28 (2H, m), 4.64-4.69 (1H, m), 5.13 (1H, dt, J=11.2 and 5.7Hz), 5.84 (1H, s), 7.08-7.16 (1H, m), 7.13 (2H, d, J=8.4Hz), 7.52 (1H, d, J=10.5Hz);
MASS (ES+): m/e 587.56 (M+1).

Example 27

Compound E27 was obtained from the Compound (96) in a manner similar to Example 1.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.79 (3H, t, J=7Hz), 1.09 (3x3H, s), 1.22 (3H, d, J=7Hz), 1.26 (3H, s), 1.45 (2H, m), 1.65 (1H, m), 1.74-1.93 (3H, m), 2.10-2.40 (6H, m), 3.11 (1H, dd, J=15 and 8Hz), 3.15 (1H, dd, J=15 and 8Hz), 3.40 (1H, m), 3.88 (1H, m), 4.21 (1H, m), 4.27 (1H, q, J=7Hz), 4.69 (1H, m), 5.24 (1H, ddd, J=9, 8 and 8Hz), 5.80 (1H, s), 6.62 (1H, d, J=16Hz), 6.87 (1H, dt, J=16, 7Hz), 6.96-7.13 (3H, m), 7.15-7.27 (2H, m), 7.30-7.48 (6H, m), 7.52 (3H, d, J=9Hz), 7.55-7.70 (4H, m);
MASS (ES-): m/e 795.

Example 28

Compound E28 was obtained from the Compound (96) in a manner similar to Example 2.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.78 (3H, t, J=7Hz), 1.09 (3x3H, s), 1.22 (3H, d, J=7Hz), 1.26 (3H, s), 1.45 (2H, m), 1.65 (1H, m), 1.72-1.92 (3H, m), 2.10-2.40 (6H, m), 3.11 (1H, dd, J=15 and 8Hz), 3.15 (1H, dd, J=15 and 8Hz), 3.40 (1H, m), 3.88 (1H, m), 4.21 (1H, m), 4.27 (1H, q, J=7Hz), 4.70 (1H, dd, J=8 and 2Hz), 5.23 (1H, ddd, J=9, 8 and 8Hz), 5.78 (1H, s), 6.61 (1H, d, J=16Hz), 6.86 (1H, dt, J=16 and 7Hz), 6.96-7.12 (3H, m), 7.15-7.28 (2H, m), 7.30-7.48 (6H, m), 7.52 (1H, d, J=9Hz), 7.55-7.69 (4H, m);
MASS (ES-): m/e 795.

Example 29

Compound E29 was obtained from the Compound (96) in a manner similar to Example 1 except that dimethyl (3R)-tert-butyldimethylsilyloxy-2-oxopentylphosphonate was used instead of dimethyl (3R)-tert-butyldimethylsilyloxy-2-oxobutylphosphonate.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.79 (3H, t, J=7Hz), 0.80 (3H, t, J=7Hz), 1.10 (3x3H, s), 1.26 (3H, s), 1.42 (2H, m), 1.55-1.70 (3H,

m), 1.72-1.91 (3H, m), 2.10-2.41 (6H, m), 3.11 (1H, dd, J=14 and 8Hz), 3.15 (1H, dd, J=14 and 8Hz), 3.41 (1H, m), 3.89 (1H, m), 4.14 (1H, q, J=7Hz), 4.21 (1H, m), 4.69 (1H, m), 5.24 (1H, ddd, J=10, 8 and 8Hz), 5.78 (1H, s), 6.55 (1H, d, J=16Hz), 6.80 (1H, dt, J=16 and 7Hz), 6.97-7.12 (3H, m), 7.15-7.27 (2H, m), 7.29-7.47 (6H, m), 7.52 (1H, d, J=10Hz), 7.55-7.67 (4H, m);
MASS (ES-): m/e 809.

Example 30

Compound E30 was obtained from the Compound E27 in a manner similar to Example 3 except that 10% palladium on carbon was used instead of $Pd-BaSO_4$.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.79 (3H, t, J=7Hz), 1.10 (3x3H, s), 1.15-1.34 (4H, m), 1.18 (3H, d, J=7Hz), 1.45 (2H, m), 1.60 (1H, m), 1.72-1.92 (3H, m), 2.08-2.40 (4H, m), 2.50 (2H, m), 3.10 (1H, dd, J=15 and 8Hz), 3.15 (1H, dd, J=15 and 7.5Hz), 3.41 (1H, m), 3.87 (1H, m), 4.18 (1H, m), 4.18 (1H, q, J=7Hz), 4.69 (1H, m), 5.23 (1H, ddd, J=10, 8 and 7.5Hz), 5.80 (1H, s), 6.96-7.08 (3H, m), 7.15-7.27 (2H, m), 7.32-7.49 (6H, m), 7.55 (1H, d, J=10Hz), 7.55-7.70 (5H, m);
MASS (ES-): m/e 797.

Example 31

Compound E31 was obtained from the Compound E30 in a manner similar to Example 3 except that 10% palladium on carbon was used instead of $Pd-BaSO_4$.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.79 (3H, t, J=7Hz), 1.10 (3x3H, s), 1.15-1.32 (4H, m), 1.18 (3H, d, J=7Hz), 1.45 (2H, m), 1.60 (1H, m), 1.71-1.92 (3H, m), 2.09-2.40 (4H, m), 2.51 (2H, t, J=7Hz), 3.10 (1H, dd, J=15 and 8Hz), 3.15 (1H, dd, J=15 and 8Hz), 3.40 (1H, m), 3.87 (1H, m), 4.18 (1H, q, J=7Hz), 4.18 (1H, m), 4.69 (1H, m), 5.23 (1H, ddd, J=10, 8 and 7.5Hz), 5.79 (1H, s), 6.95-7.09 (3H, m), 7.14-7.28 (2H, m), 7.32-7.49 (6H, m), 7.55 (1H, d, J=10Hz), 7.55-7.68 (6H, m);
MASS (ES-): m/e 797.

Example 32

Compound E32 was obtained from the Compound E29 in a manner similar to Example 3 except that 10% palladium on carbon was used instead of $Pd-BaSO_4$.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.79 (3H, t, J=7Hz), 0.81 (3H, t, J=7Hz), 1.11 (3x3H, s), 1.13-1.28 (4H, m), 1.26 (3H, s), 1.37 (2H,

m), 1.49-1.67 (3H, m), 1.71-1.92 (3H, m), 2.08-2.49 (6H, m), 3.10 (1H, dd, J=15 and 8Hz), 3.15 (1H, dd, J=15 and 7.5Hz), 3.40 (1H, m), 3.87 (1H, m), 4.10 (1H, t, J=6Hz), 4.17 (1H, m), 4.69 (1H, m), 5.23 (1H, ddd, J=9, 8 and 7.5Hz), 5.79 (1H, s), 6.96-7.08 (3H, m), 7.14-7.28 (2H, m), 7.32-7.47 (6H, m), 7.55 (1H, d, J=9Hz), 7.55-7.66 (5H, m);

MASS (ES-): m/e 811.

Example 33

Compound E33 was obtained from the Compound E30 in a manner similar to Example 6.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.80 (3H, t, J=7.5Hz), 1.24-1.42 (4H, m), 1.26 (3H, s), 1.38 (3H, d, J=7Hz), 1.54-1.70 (3H, m), 1.74-1.92 (3H, m), 2.08-2.58 (6H, m), 3.11 (1H, dd, J=15 and 8Hz), 3.15 (1H, dd, J=15 and 7Hz), 3.41 (1H, m), 3.58 (1H, d, J=5Hz), 3.87 (1H, m), 4.13-4.30 (2H, m), 4.70 (1H, m), 5.24 (1H, ddd, J=10, 8 and 7Hz), 5.84 (1H, s), 6.97-7.12 (3H, m), 7.15-7.30 (2H, m), 7.54 (1H, d, J=10Hz);

MASS (ES-): m/e 559;

MASS (ES+): m/e 561.

Example 34

Compound E34 was obtained from the Compound E31 in a manner similar to Example 6.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.80 (3H, t, J=7.5Hz), 1.20-1.42 (4H, m), 1.26 (3H, s), 1.38 (3H, d, J=7Hz), 1.53-1.73 (3H, m), 1.74-1.93 (3H, m), 2.09-2.59 (6H, m), 3.10 (1H, dd, J=15 and 8Hz), 3.15 (1H, dd, J=15 and 7Hz), 3.40 (1H, m), 3.56 (1H, d, J=5Hz), 3.87 (1H, m), 4.14-4.29 (2H, m), 4.70 (1H, m), 5.24 (1H, ddd, J=10, 8 and 7Hz), 5.83 (1H, s), 6.96-7.13 (3H, m), 7.15-7.29 (2H, m), 7.54 (1H, d, J=10Hz);

MASS (ES-): m/e 559.

Example 35

Compound E35 was obtained from the Compound E32 in a manner similar to Example 6.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.79 (3H, t, J=7.5Hz), 0.94 (3H, t, J=7.5Hz), 1.17-1.40 (4H, m), 1.26 (3H, s), 1.50-1.78 (4H, m), 1.79-1.97 (4H, m), 2.08-2.40 (6H, m), 2.45 (2H, m), 3.10 (1H, dd, J=15 and 7.5Hz), 3.14 (1H, dd, J=15 and 7.5Hz), 3.40 (1H, m), 3.51 (1H, d, J=5Hz), 3.87 (1H, m), 4.08-4.26 (2H, m), 4.70 (1H, m), 5.23 (1H, ddd, J=9, 7.5 and 7.5Hz), 5.85 (1H, s), 6.95-7.12

(3H, m), 7.14-7.31 (2H, m), 7.54 (1H, d, J=9Hz);
MASS (ES-): m/e 573;
MASS (ES+): m/e 575.

Example 36

Compound E36 was obtained from the Compound (99) in a manner similar to Example 1.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.83 (3H, t, J=7.3Hz), 1.09 (3X3H, s), 1.22 (3H, d, J=7Hz), 1.28 (3H, s), 1.38-1.52 (2H, m), 1.64 (1H, m), 1.70-1.91 (3H, m), 2.08-2.38 (6H, m), 2.94 (1H, dd, J=14 and 6Hz), 3.20 (1H, dd, J=14 and 9.5Hz), 3.28 (1H, m), 3.86 (1H, m), 4.22 (1H, m), 4.27 (1H, q, J=7Hz), 4.67 (1H, m), 5.14 (1H ,ddd, J=10, 9.5 and 6Hz), 5.87 (1H, s), 6.62 (1H, d, J=16Hz), 6.86 (1H, dt, J=16.7Hz), 7.08 (1H, d, J=10Hz), 7.16 (2X1H, d, J=8.5Hz), 7.24 (2X1H, d, J=8.5Hz), 7.31-7.48 (6H, m), 7.52-7.69 (5H, m);
MASS (ES+): m/e 813.

Example 37

Compound E37 was obtained from the Compound E36 in a manner similar to Example 3.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.83 (3H, t, J=7Hz), 1.10 (3X3H, s), 1.18 (3H, d, J=6.5Hz), 1.20-1.30 (4H, m), 1.28 (3H, s), 1.40-1.50 (2H, m), 1.60 (1H, m), 1.72-1.89 (3H, m), 2.08-2.38 (4H, m), 2.51 (2H, m), 2,94 (1H ,dd, J=14 and 6Hz), 3.20 (1H ,dd, J=14 and 10Hz), 3.28 (1H, m), 3.84 (1H, m), 4.19 (1H ,q, J=6.5Hz), 4.19 (1H, m), 4.67 (1H, m), 5.14 (1H, ddd, J=10, 10 and 6Hz), 5.87 (1H, s), 7.03 (1H, d, J=10.5Hz), 7.17 (2X1H, d, J=9Hz), 7.24 (2X1H, d, J=9Hz), 7.33-7.50 (6H, m), 7,56-7.68 (5H, m);
MASS (ES+): m/e 815.

Example 38

Compound E38 was obtained from the Compound E37 in a manner similar to Example 6.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.83 (3H, t, J=7.3Hz), 1.20-1.40 (4H, m), 1.28 (3H ,s), 1.38 (3H ,d, J=7Hz), 1.55-1.70 (3H, m), 1.72-1.90 (3H, m), 2.08-2.58 (6H, m), 2.94 (1H, dd, J=14.6Hz), 3.20 (1H, dd, J=14 and 10Hz), 3.28 (1H, m), 3.56 (1H, d, J=5Hz), 3.85 (1H, m), 4.15-4.30 (2H, m), 4.68 (1H, m), 5.14 (1H, ddd, J=10, 10 and 6Hz), 5.90 (1H, s), 7.06 (1H, d, J=10Hz), 7.17 (2X1H, d, J=9Hz), 7.24 (2X1H, d, J=9Hz), 7,58 (1H, d, J=10Hz);
MASS (ES+): m/e 577;
$[\alpha]_D^{25}$ = -116.1° (c=0.31, $CHCl_3$).

Example 39

Compound E39 was obtained from the Compound (102) in a manner similar to Example 1.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.77 (3H, t, J=7.7Hz), 0.91 (3H, t, J=7.3Hz), 1.09 (9H, s), 1.22 (3H, d, J=7.0Hz), 1.37-1.70 (4H, m), 1.71-1.92 (4H, m), 2.07-2.45 (6H, m), 2.97 (1H, dd, J=13.5 and 5.8Hz), 3.18-3.31 (2H, m), 3.83-3.95 (1H, m), 4.15-4.29 (1H, m), 4.27 (1H, q, J=6.9Hz), 4.66 (1H, br. d, J=6.9Hz), 5.12-5.24 (1H, m), 5.79 (1H, s), 6.61 (1H, d, J=15.6Hz), 6.86 (1H, dt, J=15.6 and 6.7Hz), 7.13 (1H, d, J=9.9Hz), 7.17-7.29 (5H, m), 7.30-7.45 (6H, m), 7.49 (1H, d, J=10.6Hz), 7.56-7.69 (4H, m);

MASS (ES+): m/e 793.32 (M+1).

Example 40

Compound E40 was obtained from the Compound E39 in a manner similar to Example 16.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.77 (3H, t, J=7.3Hz), 0.92 (3H, t, J=7.3Hz), 1.11 (9H, s), 1.15-1.35 (4H, m), 1.19 (3H, t, J=6.6Hz), 1.37-1.69 (5H, m), 1.70-1.91 (3H, m), 2.11-2.46 (4H, m), 2.52 (2H, dt, J=7.0 and 2.5Hz), 2.97 (1H, dd, J=13.5 and 6.3Hz), 3.18-3.31 (2H, m), 3.82-3.96 (1H, m), 4.16-4.26 (1H, m), 4.19 (1H, q, J=6.5Hz), 4.67 (1H, d, J=5.9Hz), 5.12-5.24 (1H, m), 5.79 (1H, s), 7.08 (1H, d, J=10.6Hz), 7.17-7.32 (5H, m), 7.33-7.49 (6H, m), 7.53 (1H, d, J=10.5Hz), 7.58-7.69 (4H, m);

MASS (ES+): m/e 795.09 (M+1).

Example 41

Compound E41 was obtained from the Compound E40 in a manner similar to Example 6.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.77 (3H, t, J=6.9Hz), 0.91 (3H, t, J=7.3Hz), 1.21-1.41 (4H, m), 1.38 (3H, d, J=7.0Hz), 1.51-1.70 (4H, m), 1.70-1.92 (4H, m), 2.08-2.58 (6H, m), 2.96 (1H, dd, J=13.6 and 6.4Hz), 3.16-3.30 (2H, m), 3.56 (1H, d, J=4.6Hz), 3.82-3.94 (1H, m), 4.13-4.29 (2H, m), 4.67 (1H, br. d, J=6.2Hz), 5.11-5.24 (1H, m), 5.81 (1H, s), 7.11 (1H, d, J=10.3Hz), 7.16-7.34 (5H, m), 7.50 (1H, d, J=10.4Hz);

MASS (ES+): m/e 557.29 (M+1).

Example 42

Compound E42 was obtained from the Compound (105) in a manner similar to Example 1.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.83 (3H, t, J=7.5Hz), 1.09 (3x3H, s),

1.22 (3H, d, J=7Hz), 1.28 (3H, s), 1.45 (2H, m), 1.56-1.90 (4H, m), 2.07-2.40 (6H, m), 2.97 (1H, dd, J=13.5 and 6.5Hz), 3.24 (1H, dd, J=13.5 and 9Hz), 3.27 (1H, m), 3.87 (1H, m), 4.21 (1H, m), 4.27 (1H, q, J=7Hz), 4.64 (1H, m), 5.19 (1H, ddd, J=10, 9 and 6.5Hz), 5.81 (1H, s), 6.62 (1H, br-d, J=16Hz), 6.87 (1H, dt, J=16, 7Hz), 7.13 (1H, d, J=10Hz), 7.17-7.49 (11H, m), 7.53 (1H, d, J=10Hz), 7.56-7.76 (4H, m);

MASS (ES-): m/e 777.

Example 43

Compound E43 was obtained from the Compound (105) in a manner similar to Example 2.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.82 (3H, t, J=7.3Hz), 1.09 (3x3H, s), 1.23 (3H, d, J=7Hz), 1.28 (3H, s), 1.45 (2H, m), 1.58-1.92 (4H, m), 2.08-2.40 (6H, m), 2.97 (1H, dd, J=13.5 and 6Hz), 3.24 (1H, dd, J=13.5 and 9.5Hz), 3.27 (1H, m), 3.87 (1H, m), 4.21 (1H, dt, J=10 and 7.5Hz), 4.27 (1H, q, J=7Hz), 4.67 (1H, dd, J=8 and 2.5Hz), 5.19 (1H, ddd, J=10, 9.5 and 6Hz), 5.81 (1H, s), 6.61 (1H, br-d, J=16Hz), 6.87 (1H, dt, J=16 and 7Hz), 7.13 (1H, d, J=10.5Hz), 7.16-7.49 (11H, m), 7.53 (1H, d, J=10Hz), 7.56-7.69 (4H, m);

MASS (ES-): m/e 777.

Example 44

Compound E44 was obtained from the Compound (105) in a manner similar to Example 29.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.80 (3H, t, J=7.4Hz), 0.83 (3H, t, J=7.4Hz), 1.10 (3x3H, s), 1.28 (3H, s), 1.44 (2H, m), 1.54-1.90 (6H, m), 2.08-2.40 (6H, m), 2.97 (1H, dd, J=14 and 6Hz), 3.24 (1H, dd, J=14 and 9.5Hz), 3.27 (1H, m), 3.87 (1H, m), 4.15 (1H, t, J=6Hz), 4.20 (1H, m), 4.67 (1H, m), 5.19 (1H, ddd, J=10, 9.5 and 6Hz), 5.78 (1H, s), 6.55 (1H, d, J=16Hz), 6.80 (1H, dt, J=16 and 7Hz), 7.12 (1H, d, J=10.5Hz), 7.16-7.47 (11H, m), 7.53 (1H, d, J=10Hz), 7.53-7.68 (4H, m);

MASS (ES-): m/e 791.

Example 45

Compound E45 was obtained from the Compound E42 in a manner similar to Example 16.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.83 (3H, t, J=7.3Hz), 1.10 (3x3H, s), 1.18 (3H, d, J=7Hz), 1.20-1.33 (4H, m), 1.28 (3H, s), 1.45 (2H, m), 1.60 (1H, m), 1.71-1.90 (3H, m), 2.08-2.40 (4H, m), 2.51 (2H,

m), 2.97 (1H, dd, J=13.5 and 6Hz), 3.24 (1H, dd, J=13.5 and 9Hz), 3.27 (1H, m), 3.86 (1H, m), 4.18 (1H, m), 4.18 (1H, q, J=7Hz), 4.67 (1H, m), 5.18 (1H, ddd, J=10, 9 and 6Hz), 5.81 (1H, s), 7.07 (1H, d, J=10.5Hz), 7.16-7.31 (5H, m), 7.33-7.48 (6H, m), 7.57 (1H, d, J=10Hz), 7.58-7.74 (4H, m);

MASS (ES-): m/e 779.

Example 46

Compound E46 was obtained from the Compound E43 in a manner similar to Example 16.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.83 (3H, t, J=7.3Hz), 1.10 (3x3H, s), 1.16-1.33 (4H, m), 1.18 (3H, d, J=7Hz), 1.28 (3H, s), 1.46 (2H, m), 1.58 (1H, m), 1.68-1.88 (3H, m), 2.07-2.40 (4H, m), 2.51 (2H, t, J=7Hz), 2.97 (1H, dd, J=13.5 and 6Hz), 3.24 (1H, dd, J=13.5 and 9.5Hz), 3.27 (1H, m), 3.86 (1H, m), 4.18 (1H, m), 4.18 (1H, q, J=7Hz), 4.67 (1H, dd, J=8 and 2.5Hz), 5.18 (1H, ddd, J=10, 9.5 and 6Hz), 5.82 (1H, s), 7.08 (1H, d J=10Hz), 7.16-7.32 (5H, m), 7.33-7.50 (6H, m), 7.58 (1H, d, J=10Hz), 7.58-7.70 (5H, m);

MASS (ES-): m/e 779.

Example 47

Compound E47 was obtained from the Compound E44 in a manner similar to Example 16.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.81 (3H, t, J=7Hz), 0.83 (3H, t, J=7Hz), 1.11 (9H, s), 1.15-1.26 (4H, m), 1.28 (3H, s), 1.30-1.46 (2H, m), 1.50-1.85 (6H, m), 2.07-2.48 (6H, m), 2.97 (1H, dd, J=14 and 6Hz), 3.24 (1H, dd, J=14 and 9Hz), 3.26 (1H, m), 3.86 (1H, m), 4.10-4.23 (2H, m), 4.67 (1H, m), 5.19 (1H, m), 5.80 (1H, s), 7.06 (1H, d, J=10.5Hz); 7.16-7.31 (5H, m), 7.32-7.47 (6H, m), 7.54-7.66 (5H, m);

MASS: (ES+) m/e 795.

Example 48

Compound E48 was obtained from the Compound E44 in a manner similar to Example 6 except that pyridine hydrofluoride was used instead of tetrabutylammonium fluoride.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.83 (3H, t, J=7Hz), 0.94 (3H, t, J=7Hz), 1.20-1.97 (8H, m), 1.29 (3H, s), 2.08-2.40 (6H, m), 2.97 (1H, dd, J=14 and 6Hz), 3.23 (1H, dd, J=14 and 9Hz), 3.26 (1H, m), 3.59 (1H, d, J=5Hz), 3.87 (1H, m), 4.22 (1H, m), 4.67 (1H, m), 5.19 (1H, ddd, J=10, 9 and 6Hz), 5.84 (1H, s), 6.26 (1H, d, J=16Hz), 7.00 (1H, dt, J=16 and 7Hz), 7.16 (1H, d, J=10Hz), 7.19-

7.32 (5H, m), 7.50 (1H, d, J=10Hz);
MASS: (ES-) m/e 553.

Example 49

Compound E49 was obtained from the Compound E47 in a manner similar to Example 48.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.83 (3H, t, J=7Hz), 0.94 (3H, t, J=7Hz), 1.22-1.40 (4H, m), 1.28 (3H, s), 1.52-1.70 (4H, m), 1.71-1.98 (4H, m), 2.08-2.24 (2H, m), 2.25-2.40 (2H, m), 2.45 (2H, m), 2.96 (1H, ddd, J=13, 6 and 5Hz), 3.18-3.32 (2H, m), 3.50 (1H, d, J=5Hz), 3.86 (1H, m), 4.14 (1H, m), 4.20 (1H, m), 4.67 (1H, m), 5.19 (1H, ddd, J=10, 9 and 6Hz), 5.82 (1H, s), 7.10 (1H, d, J=10Hz), 7.16-7.32 (5H, m), 7.54 (1H, d, J=10Hz);
MASS (ES+): m/e 557.

Example 50

Compound 50 was obtained from the Compound E42 in a manner similar to Example 48.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.83 (3H, t, J=7.3Hz), 1.29 (3H, s), 1.38 (3H, d, J=7Hz), 1.42-1.93 (6H, m), 2.07-2.40 (6H, m), 2.97 (1H, dd, J=13.5 and 6Hz), 3.24 (1H, dd, J=13.5 and 9.5Hz), 3.26 (1H, m), 3.65 (1H, d, J=5Hz), 3.87 (1H, m), 4.22 (1H, dt, J=10.5 and 7.5Hz), 4.44 (1H, dq, J=7 and 5Hz), 4.67 (1H, dd, J=8 and 2.5Hz), 5.19 (1H, ddd, J=10, 9.5 and 6Hz), 5.84 (1H, s), 6.24 (1H, br-d, J=16Hz), 7.01 (1H, dt, J=16 and 7Hz), 7.16 (1H, d, J=10.5Hz), 7.16-7.32 (5H, m), 7.50 (1H, d, J=10Hz);
MASS (ES-): m/e 539.

Example 51

Compound E51 was obtained from the Compound E45 in a manner similar to Example 48.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.83 (3H, t, J=7.3Hz), 1.20-1.42 (4H, m), 1.28 (3H, s), 1.38 (3H, d, J=7Hz), 1.54-1.90 (6H, m), 2.08-2.58 (6H, m), 2.96 (1H, dd, J=13.5 and 6Hz), 3.24 (1H, dd, J=13.5 and 9Hz), 3.27 (1H, m), 3.57 (1H, d, J=4.5Hz), 3.86 (1H, m), 4.14-4.29 (2H, m), 4.67 (1H, dd, J=8 and 2.5Hz), 5.19 (1H, ddd, J=10, 9 and 6Hz), 5.82 (1H, s), 7.10 (1H, d, J=10Hz), 7.16-7.33 (5H, m), 7.55 (1H, d, J=10Hz), 3.57 (1H, d, J=4.5Hz);
MASS (ES-): m/e 541.

Example 52

Compound E52 was obtained from the Compound E46 in a manner similar to Example 48.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.83 (3H, t, J=7.5Hz), 1.20-1.41 (4H, m), 1.28 (3H, s), 1.38 (3H, d, J=7Hz), 1.52-1.90 (6H, m), 2.08-2.58 (6H, m), 2.96 (1H, dd, J=13.5 and 6Hz), 3.24 (1H, dd, J=13.5 and 9.5Hz), 3.27 (1H, m), 3.57 (1H, d, J=5Hz), 3.86 (1H, m), 4.14-4.29 (2H, m), 4.67 (1H, dd, J=8 and 2.5Hz), 5.18 (1H, ddd, J=10, 9.5 and 6Hz), 5.83 (1H, s), 7.10 (1H, d, J=10Hz), 7.16-7.31 (5H, m), 7.55 (1H, d, J=10Hz);
MASS (ES-): m/e 541.

Example 53

To a solution of Compound E52 (7.7 mg) in pyridine (0.8 ml) was added (R)-(-)-α-methoxy-α-trifluoromethyl-α-phenylacetyl chloride (7.7 mg) at 0°C and the mixture was stirred at ambient temperature until the Compound E52 was disappeared. The solvent was evaporated and the residue was purified by preparative thin layer chromatography (hexane/ethyl acetate = 1:3 v/v) to give Compound E53 as an oil (8.4 mg).

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.83 (3H, t, J=7.3Hz), 1.20-1.38 (4H, m), 1.28 (3H, s), 1.44 (3H, d, J=7Hz), 1.54-1.90 (6H, m), 2.08-2.59 (6H, m), 2.97 (1H, dd, J=13.5 and 6Hz), 3.24 (1H, dd, J=13.5 and 9.5Hz), 3.28 (1H, m), 3.63 (3H, s), 3.88 (1H, m), 4.14-4.25 (2H, m), 4.67 (1H, dd, J=8.5 and 3Hz), 5.19 (1H, ddd, J=10, 9.5 and 6Hz), 5.24 (1H, q, J=7Hz), 5.81 (1H, s), 7.09 (1H, d, J=10Hz), 7.16-7.32 (5H, m), 7.40-7.48 (3H, m), 7.56 (1H, d, J=10Hz), 7.59-7.66 (2H, m);
MASS: (ES-) m/e 757.

Example 54

Compound E54 was obtained from the Compound E52 in a manner similar to Example 53 except that (S)-(-)-α-methoxy-α-trifluoromethyl-α-phenylacetyl chloride was used instead of (R)-(-)-α-methoxy-α-trifluoromethyl-α-phenylacetyl chloride.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.83 (3H, t, J=7.3Hz), 1.18-1.38 (4H, m), 1,28 (3H, s), 1,46-1.87 (6H, m), 1.49 (3H, d, J=7Hz), 2.09-2.48 (6H, m), 2.96 (1H, dd, J=13.5 and 6Hz), 3.24 (1H, dd, J=13.5 and 9.5Hz), 3.27 (1H, m), 3.58 (3H ,s), 3.86 (1H, m), 4.12-4.26 (2H, m), 4.67 (1H, dd, J=8.2Hz), 5.18 (1H, m), 5.28 (1H, q, J=7Hz), 5.81 (1H, s), 7.08 (1H, d, J=10.5Hz), 7.16-7.32 (5H, m), 7.40-7.47 (3H, m), 7.51-7.62 (3H, m);
MASS (ES-): m/e 757.

Example 55

Compound E55 was obtained from the Compound 51 in a manner similar to Example 45.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.83 (3H, t, J=7.5Hz), 1.17-1.34 (4H, m), 1.28 (3H, s), 1.49 (3H, d, J=7Hz), 1.51-1.63 (3H, m), 1.70-1.88 (3H, m), 2.08-2.50 (6H, m), 2.96 (1H, dd, J=13.5 and 6.5Hz), 3.23 (1H, dd, J=13.5 and 9.5Hz), 3.27 (1H, m), 3.58 (3H, s), 3.86 (1H, m), 4.18 (1H, m), 4.67 (1H, m), 5.18 (1H, m), 5.29 (1H, q, J=7Hz), 5.80 (1H, s), 7.08 (1H, d, J=10Hz), 7.16-7.32 (5H, m), 7.40-7.47 (3H, m), 7.51-7.64 (3H, m);

MASS (ES-): m/e 757.

Example 56

Compound E56 was obtained from the Compound 51 in a manner similar to Example 46.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.83 (3H, t, J=7.4Hz), 1.17-1.37 (4H, m), 1.28 (3H, s), 1.44 (3H, d, J=7Hz), 1.52-1.68 (3H, m), 1.70-1.90 (3H, m), 2.08-2.59 (6H, m), 2.97 (1H, dd, J=13.5 and 6Hz), 3.24 (1H, dd, J=13.5 and 10Hz), 3.27 (1H, m), 3.63 (3H, s), 3.86 (1H, m), 4.19 (1H, dt, J=10 and 7.5Hz), 4.67 (1H, dd, J=8 and 2Hz), 5.18 (1H, ddd, J=10, 10 and 6Hz), 5.25 (1H, q, J=7Hz), 5.81 (1H, s), 7.09 (1H, d, J=10Hz), 7.16-7.32 (5H, m), 7.40-7.48 (3H, m), 7.52-7.66 (2H, m), 7.56 (1H, d, J=10Hz);

MASS (ES-): m/e 757.

Example 57

Compound E57 was obtained in a manner similar to Example 1.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.89 (3H, t, J=7.0Hz), 0.96 (3H, t, J=6.5Hz), 1.09 (9H, s), 1.17-1.89 (12H, m), 1.23 (3H, d, J=6.9Hz), 1.99-2.44 (6H, m), 2.98 (1H, dd, J=13.5 and 6.5Hz), 3.20-3.32 (1H, m), 3.23 (1H, dd, J=13.5 and 9.5Hz), 3.80-3.93 (1H, m), 4.12-4.27 (1H, m), 4.27 (1H, q, J=7.0Hz), 4.67 (1H, br.d, J=5.5Hz), 5.10-5.23 (1H, m), 5.79 (1H, s), 6.61 (1H, d, J=15.8Hz), 6.87 (1H, dt, J=15.8 and 6.7Hz), 7.12 (1H, d, J=10.3Hz), 7.16-7.29 (5H, m), 7.29-7.45 (6H, m), 7.48 (1H, d, J=11.0Hz), 7.55-7.74 (4H, m);

MASS (ES+): m/e 821.39 (M+1).

Example 58

Compound E58 was obtained from the Compound E57 in a manner similar to Example 16.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.89 (3H, t, J=6.9Hz), 0.97 (3H, t, J=7.0Hz), 1.11 (9H, s), 1.16-1.67 (12H, m), 1.19 (3H, d, J=7.0Hz), 1.68-1.88

(4H, m), 2.00-2.45 (4H, m), 2.51 (2H, br. t, J=6.9Hz), 2.98 (1H, dd, J=13.1 and 6.3Hz), 3.21-3.32 (1H, m), 3.23 (1H, dd, J=13.1 and 9.2Hz), 3.81-3.92 (1H, m), 4.13 (1H, q, J=7.1Hz), 4.15-4.23 (1H, m), 4.68 (1H, br. d, J=5.7Hz), 5.10-5.22 (1H, m), 5.80 (1H, s), 7.07 (1H, d, J=10.3Hz), 7.16-7.31 (6H, m), 7.33-7.48 (5H, m), 7.52 (1H, d, J=10.2Hz), 7.58-7.75 (4H, m);

MASS (ES+): m/e 823.31 (M+1).

Example 59

Compound E59 was obtained from the Compound E57 in a manner similar to Example 6.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.89 (3H, t, J=6.5Hz), 0.96 (3H, t, J=6.9Hz), 1.12-1.41 (7H, m), 1.38 (3H, d, J=7.4Hz), 1.41-1.69 (5H, m), 1.70-1.88 (4H, m), 2.00-2.58 (6H, m), 2.98 (1H, dd, J=12.5 and 6.2Hz), 3.19-3.31 (1H, m), 4.12-4.29 (1H, dd, J=12.5 and 9.0Hz), 3.55 (1H, d, J=4.8Hz), 3.80-3.93 (1H, m), 4.12-4.29 (2H, m), 4.67 (1H, br.d, J=5.4Hz), 5.10-5.22 (1H, m), 5.81 (1H, s), 7.10 (1H, d, J=9.9Hz), 7.16-7.32 (5H, m), 7.49 (1H, d, J=10.5Hz);

MASS (ES+): m/e 585.34 (M+1).

Example 60

Compound E60 was obtained in a manner similar to Example 3.

Example 61

A solution of the Compound E60 (88 mg) in methanol (3 ml) was hydrogenated in the presence of palladium hydroxide, 20 wt% Pd (dry basis) on carbon (Pearlman's catalyst) (30 mg) for 2 hours. The catalyst was filtered off and the filtrate was concentrated in vacuo. The residue was purified by preparative thin layer chromatography (eluted with chloroform : methanol = 20:1 v/v) to give Compound E61 as an amorphous (76 mg).

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.04 (3x3H, s), 1.22-1.43 (4H, m), 1.38 (3H, d, J=7Hz), 1.56-1.93 (6H, m), 2.17 (1H, m), 2.26-2.58 (3H, m), 2.91 (1H, dd, J=13 and 5Hz), 3.02 (1H, m), 3.19 (1H, dd, J=13 and 11Hz), 3.57 (1H, d, J=5Hz), 3.91 (1H, m), 4.13 (1H, d, J=10.5Hz), 4.24 (1H, dq, J=7 and 5Hz), 4.33 (1H, dt, J=10 and 7.5Hz), 4.60 (1H, m), 5.02 (1H, ddd, J=11, 10 and 5Hz), 6.23 (1H, d, J=10.5Hz), 6.25 (1H, d, J=10Hz), 7.12-7.32 (6H, m);

MASS: (ES+): m/e 557.

Example 62

Compound E62 was obtained in a manner similar to Example 1.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.71 (3H, d, J=6.9Hz), 0.87 (3H, d, J=6.6Hz),

1.09 (9H, s), 1.15 (3H, s), 1.36-1.92 (10H, m), 2.13-2.37 (3H, m), 2.99 (1H, dd, J=13.9 and 7.0Hz), 3.21 (1H, dd, J=13.9 and 8.8Hz), 3.26-3.36 (2H, m), 3.83-3.93 (1H, m), 4.17-4.31 (2H, m), 4.66-4.72 (1H, m), 5.21 (1H, ddd, J=10.6, 8.8 and 7.0Hz), 5.78 (1H, s), 6.61 (1H, d, J=15.8Hz), 6.87 (1H, dt, J=15.8 and 6.6Hz), 7.13 (1H, d, J=10.6Hz), 7.16-7.50 (10H, m), 7.54-7.74 (6H, m);
MASS: (ES+): m/e 793.32 (M+1).

Example 63

Compound E63 was obtained in a manner similar to Example 4.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.70 (3H, d, J=7.0Hz), 0.87 (3H, d, J=6.6Hz), 1.10 (9H, s), 1.15 (3H, s), 1.18 (3H, d, J=6.6Hz), 1.21-1.88 (11H, m), 2.14-2.37 (2H, m), 2.51 (2H, dt, J=7.3 and 2.2Hz), 2.99 (1H, dd, J=13.9 and 7.0Hz), 3.20 (1H, dd, J=13.9 and 8.8Hz), 3.26-3.37 (1H, m), 3.82-3.92 (1H, m), 4.13-4.27 (2H, m), 4.66-4.71 (1H, m), 5.20 (1H, ddd, J=10.3, 8.8 and 7.0Hz), 5.77 (1H, s), 7.07 (1H, d, J=10.3Hz), 7.16-7.31 (5H, m), 7.33-7.48 (5H, m), 7.58-7.74 (6H, m);
MASS: (ES+): m/e 795.29 (M+1).

Example 64

Compound E64 was obtained in a manner similar to Example 6.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.71 (3H, d, J=7.0Hz), 0.88 (3H, d, J=6.6Hz), 1.15 (3H, s), 1.21-1.43 (4H, m), 1.38 (3H, d, J=7.0Hz), 1.52-1.72 (3H, m), 1.72-1.91 (3H, m), 2.11-2.57 (4H, m), 2.99 (1H, dd, J=13.6 and 7.0Hz), 3.20 (1H, dd, J=13.6 and 8.8Hz), 3.26-3.38 (2H, m), 3.57 (1H, brs), 3.83-3.93 (1H, m), 4.16-4.28 (2H, m), 4.66-4.73 (1H, m), 5.15-5.26 (1H, m), 5.85 (1H, s), 7.12 (1H, d, J=10.3Hz), 7.16-7.32 (5H, m), 7.61 (1H, d, J=10.3Hz);
MASS: (ES+): m/e 557.39 (M+1).

Example 65

Compound E65 was obtained in a manner similar to Example 1.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.08 (9H, s), 1.21 (3H, d, J=7.0Hz), 1.32-1.84 (7H, m), 2.10-2.39 (3H, m), 2.85 (1H, dd, J=13.6 and 10.6Hz), 3.00 (1H, dd, J=14.3 and 7.0Hz), 3.04-3.15 (1H, m), 3.18 (1H, dd, J=13.6 and 10.6Hz), 3.39 (1H, dd, J=14.3 and 8.4Hz), 3.91-4.01 (1H, m), 4.21-4.32 (1H, m), 4.26 (1H, q, J=7.0Hz), 4.59-4.64 (1H, m), 4.81-4.91 (1H, m), 5.06 (1H, dt, J=10.6 and 5.1Hz), 6.32 (1H, d, J=9.9Hz), 6.45 (1H, d, J=10.6Hz), 6.57 (1H, d, J=15.8Hz), 6.82 (1H, dt, J=15.8 and 7.0Hz), 7.13-7.27 (5H, m), 7.29-7.50 (10H, m), 7.55-7.68 (5H, m), 7.74-7.83 (3H, m);
MASS: (ES-): m/e 875.40 (M-1).

Example 66

Compound E66 was obtained in a manner similar to Example 4. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.10 (9H, s), 1.13-1.26 (4H, m), 1.18 (3H, d, J=7.0Hz), 1.34-1.46 (2H, m), 1.54-1.81 (4H, m), 2.15-2.41 (2H, m), 2.46 (2H, dt, J=7.3 and 1.8Hz), 2.85 (1H, dd, J=13.2 and 5.1Hz), 3.00 (1H, dd, J=13.9 and 7.3Hz), 3.04-3.15 (1H, m), 3.18 (1H, dd, J=13.2 and 10.6Hz), 3.39 (1H, dd, J=13.9 and 8.4Hz), 3.90-4.00 (1H, m), 4.17 (1H, q, J=7.0Hz), 4.18-4.29 (1H, m), 4.58-4.64 (1H, m), 4.81-4,91 (1H, m), 5.06 (1H, dt, J=10.6 and 5.1Hz), 6.30 (1H, d, J=9.9Hz), 6.46 (1H, d, J=10.6Hz), 7.09-7.27 (5H, m), 7.31-7.48 (10H, m), 7.58-7.68 (5H, m), 7.74-7.82 (3H, m);

MASS: (ES+): m/e 879.31 (M+1).

Example 67

Compound E67 was obtained in a manner similar to Example 6. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.16-1.40 (4H, m), 1.36 (3H, d, J=7.0Hz), 1.47-1.87 (6H, m), 2.14-2.51 (4H, m), 2.86 (1H, dd, J=13.6 and 5.5Hz), 3.02 (1H, dd, J=14.3 and 7.3Hz), 3.06-3.14 (1H, m), 3.19 (1H, dd, J=13.6 and 10.6Hz), 3.39 (1H, dd, J=14.3 and 8.4Hz), 3.56 (1H, br), 3.91-4.01 (1H, m), 4.16-4.31 (2H, m), 4.59-4.66 (1H, m), 4.81-4.92 (1H, m), 5.08 (1H, dt, J=10.6 and 5.5Hz), 6.32 (1H, d, J=9.9Hz), 6.47 (1H, d, J=10.6Hz), 7.11-7.30 (6H, m), 7.35 (1H, dd, J=8.4 and 1.5Hz), 7.41-7.51 (2H, m), 7.67 (1H, s), 7.74-7.84 (3H, m);

MASS: (ES+): m/e 641.32 (M+1).

Example 68

Compound E68 was obtained in a manner similar to Example 1. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.08 (9H, s), 1.22 (3H, d, J=7.0Hz), 1.30-1.85 (7H, m), 2.11-2.26 (2H, m), 2.29-2.38 (1H, m), 2.86 (1H, d, J=16.5Hz), 2.94 (1H, dd, J=13.2 and 5.3Hz), 3.11-3.22 (1H, m), 3.31 (1H, dd, J=13.2 and 10.3Hz), 3.62 (1H, d, J=16.5Hz), 3.90-4.02 (3H, m), 4.16-4.27 (1H, m), 4.27 (1H, q, J=7Hz), 4.64-4.70 (1H, m), 5.15 (1H, dt, J=10.3 and 5.3Hz), 6.32 (1H, s), 6.58 (1H, d, J=15.8Hz), 6.84 (1H, dt, J=15.8 and 6.8Hz), 7.15-7.29 (10H, m), 7.29-7.46 (6H, m), 7.50 (1H, d, J=10.3Hz), 7.55-7.75 (4H, m);

MASS: (ES+): m/e 839.28 (M+1).

Example 69

Compound E69 was obtained in a manner similar to Example 4. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.10 (9H, s), 1.18 (3H, d, J=7.0Hz), 1.15-1.35 (2H, m), 1.36-1.49 (1H, m), 1.54-1.84 (7H, m), 2.10-2.41 (2H, m), 2.49 (2H, dt, J=7.7 and 2.6Hz), 2.85 (1H, d, J=15.8Hz), 2.93 (1H, dd, J=13.2

and 5.1Hz), 3.11-3.22 (1H, m), 3.30 (1H, dd, J=13.2 and 10.3Hz), 3.62 (1H, d, J=16.5Hz), 3.89-3.99 (1H, m), 3.97 (1H, d, J=16.5Hz), 3.98 (1H, d, J=15.8Hz), 4.13-4.24 (1H, m), 4.15 (1H, q, J=7.0Hz), 4.64-4.70 (1H, m), 5.14 (1H, dt, J=10.3 and 5.1Hz), 6.32 (1H, s), 7.12-7.31 (10H, m), 7.32-7.47 (6H, m), 7.53 (1H, d, J=10.3Hz), 7.58-7.68 (4H, m);
MASS: (ES+): m/e 841.22 (M+1).

Example 70

Compound E70 was obtained in a manner similar to Example 6.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.37 (3H, d, J=7.0Hz), 1.51-1.86 (9H, m), 2.06-2.26 (2H, m), 2.27-2.54 (3H, m), 2.86 (1H, d, J=16.2Hz), 2.92 (1H, dd, J=13.2 and 5.1Hz), 3.09-3.21 (1H, m), 3.29 (1H, dd, J=13.2 and 10.3Hz), 3.55 (1H, d, J=4.5Hz), 3.60 (1H, d, J=16.2Hz), 3.88-4.02 (1H, m), 3.97 (2H, d, J=16.2Hz), 4.13-4.27 (2H, m), 4.63-4.70 (1H, m), 5.14 (1H, dt, J=10.3 and 5.1Hz), 6.39 (1H, s), 7.13-7.31 (10H, m), 7.51 (1H, d, J=10.3Hz);
MASS: (ES+): m/e 603.35 (M+1).

Example 71

Compound E71 was obtained in a manner similar to Example 1.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.83 (3H, t, J=7.0Hz), 1.10 (9H, s), 1.23 (3H, d, J=7.0Hz), 1.29 (3H, s), 1.39-1.91 (8H, m), 2.08-2.38 (4H, m), 3.13 (1H, dd, J=13.2 and 6.2Hz), 3.20-3.29 (1H, m), 3.42 (1H, dd, J=13.2 and 9.9Hz), 3.84-3.93 (1H, m), 4.17-4.27 (1H, m), 4.28 (1H, q, J=7.0Hz), 4.62-4.68 (1H, m), 5.30 (1H, dt, J=9.9 and 6.2Hz), 5.87 (1H, s), 6.62 (1H, d, J=15.4Hz), 6.88 (1H, dt, J=15.4 and 6.6Hz), 7.15 (1H, d, J=9.9Hz), 7.31-7.49 (9H, m), 7.57-7.74 (6H, m), 7.74-7.83 (3H, m);
MASS: (ES+): m/e 829.43 (M+1).

Example 72

Compound E72 was obtained in a manner similar to Example 4.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.83 (3H, t, J=7.3Hz), 1.00-1.34 (4H, m), 1.10 (9H, s), 1.19 (3H, d, J=6.6Hz), 1.28 (3H, s), 1.35-1.89 (12H, m), 2.07-2.40 (4H, m), 2.51 (2H, dt, J=7.3 and 2.2Hz), 3.12 (1H, dd, J=13.6 and 5.9Hz), 3.18-3.30 (1H, m), 3.41 (1H, dd, J=13.6 and 9.9Hz), 3.81-3.92 (1H, m), 4.12-4.27 (3H, m), 4.61-4.67 (1H, m), 5.29 (1H, dt, J=9.9 and 5.9Hz), 5.83 (1H, s), 7.08 (1H, d, J=10.3Hz), 7.32-7.49 (9H, m), 7.57-7.73 (6H, m), 7.73-7.83 (3H, m);
MASS: (ES+): m/e 831.35 (M+1).

Example 73

Compound E73 was obtained in a manner similar to Example 6.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.83 (3H, t, J=7.3Hz), 1.20-1.40 (4H, m),

1.29 (3H, s), 1.38 (3H, d, J=7.0Hz), 1.52-1.90 (6H, m), 2.07-2.57 (6H, m), 3.12 (1H, dd, J=13.6 and 5.9Hz), 3.19-3.29 (1H, m), 3.41 (1H, dd, J=13.6 and 9.9Hz), 3.56 (1H, d, J=4.8Hz), 3.82-3.92 (1H, m), 4.15-4.29 (2H, m), 4.62-4.68 (1H, m), 5.30 (1H, dt, J=9.9 and 5.9Hz), 5.88 (1H, s), 7.11 (1H, d, J=10.3Hz), 7.35-7.40 (1H, m), 7.40-7.49 (2H, m), 7.62 (1H, d, J=10.3Hz), 7.69 (1H, s), 7.74-7.83 (3H, m);
MASS: (ES+): m/e 593.35 (M+1).

Example 74

Compound E74 was obtained in a manner similar to Example 1.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.10 (9H, s), 1.15-1.88 (5H, m), 1.19-1.29 (3H, m), 2.14-2.37 (4H, m), 2.86 (1H, dd, J=13.2 and 5.1Hz), 2.98 (1H, dd, J=14.7 and 5.9Hz), 3.05-3.16 (1H, m), 3.18 (1H, dd, J=13.2 and 10.6Hz), 3.35 (1H, dd, J=14.7 and 8.8Hz), 3.77 (3H, s), 3.93-4.02 (1H, m), 4.21-4.33 (3H, m), 4.59-4.64 (1H, m), 4.81 (1H, dt, J=9.5 and 6.6Hz), 5.08 (1H, dt, J=10.6 and 5.1Hz), 6.36 (1H, d, J=9.9Hz), 6.45 (1H, d, J=10.6Hz), 6.58 (1H, d, J=15.4Hz), 6.84 (1H, dt, J=15.4 and 7.0Hz), 6.87 (1H, s), 7.08-7.26 (7H, m), 7.32-7.49 (7H, m), 7.56-7.68 (6H, m);
MASS (ES-) m/e 878.36 (M-1).

Example 75

Compound E75 was obtained in a manner similar to Example 4.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.10 (9H, s), 1.13-1.32 (3H, m), 1.38-1.50 (2H, m), 1.54-1.84 (5H, m), 2.16-2.38 (4H, m), 2.45-2.53 (2H, m), 2.86 (1H, dd, J=13.2 and 5.1Hz), 2.99 (1H, dd, J=14.7 and 5.9Hz), 3.05-3.16 (1H, m), 3.18 (1H, dd, J=13.2 and 10.6Hz), 3.35 (1H, dd, J=14.7 and 9.5Hz), 3.77 (3H, s), 3.92-4.01 (1H, m), 4.14-4.24 (1H, m), 4.26 (2H, q, J=7.0Hz), 4.59-4.64 (1H, m), 4.82 (1H, dt, J=9.5 and 5.9Hz), 5.08 (1H, dt, J=10.6 and 5.1Hz), 6.34 (1H, d, J=9.9Hz), 6.47 (1H, d, J=10.6Hz), 6.87 (1H, s), 7.09-7.31 (7H, m), 7.33-7.49 (7H, m), 7.58-7.67 (6H, m);
MASS (ES+): m/e 882.37 (M+1).

Example 76

Compound E76 was obtained in a manner similar to Example 6.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.19-1.40 (4H, m), 1.38 (3H, d, J=7.0Hz), 1.50-1.86 (6H, m), 2.13-2.55 (4H, m), 2.85 (1H, dd, J=13.6 and 5.1Hz), 2.98 (1H, dd, J=14.7 and 6.6Hz), 3.04-3.15 (1H, m), 3.17 (1H, dd, J=13.6 and 10.6Hz), 3.34 (1H, dd, J=14.7 and 8.8Hz), 3.52-3.59 (1H, m), 3.73 (3H, s), 3.92-4.01 (1H, m), 4.17-4.31 (2H, m), 4.58-4.65 (1H, m), 4.81 (1H, ddd, J=9.5, 8.8 and 6.6Hz), 5.08 (1H, dt, J=10.6 and 5.1Hz), 6.34

(1H, d, J=9.5Hz), 6.46 (1H, d, J=10.6Hz), 6.87 (1H, s), 7.08-7.31 (9H, m), 7.60 (1H, d, J=8.1Hz);
MASS (ES+): m/e 644.48 (M+1).

Example 77

Compound E77 was obtained in a manner similar to Example 1. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (3H, t, J=7.3Hz), 1.09 (9H, s), 1.22 (3H, d, J=7.0Hz), 1.28 (3H, s), 1.38-1.91 (7H, m), 2.08-2.39 (5H, m), 2.30 (3H, s), 2.91 (1H, dd, J=13.6 and 6.2Hz), 3.20 (1H, dd, J=13.6 and 10.3Hz), 3.23-3.33 (1H, m), 3.82-3.92 (1H, m), 4.16-4.25 (1H, m), 4.27 (1H, q, J=6.6Hz), 4.64-4.70 (1H, m), 5.16 (1H, dt, J=10.3 and 6.2Hz), 5.84 (1H, s), 6.61 (1H, d, J=15.7Hz), 6.87 (1H, dt, J=15.7 and 6.6Hz), 7.05-7.13 (4H, m), 7.14 (1H, d, J=9.5Hz), 7.31-7.45 (6H, m), 7.51 (1H, d, J=10.3Hz), 7.56-7.68 (4H, m);
MASS (ES+): m/e 793.57 (M+1).

Example 78

Compound E78 was obtained in a manner similar to Example 4. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (3H, t, J=7.7Hz), 1.10 (9H, s), 1.18 (3H, d, J=6.6Hz), 1.28 (3H, s), 1.38-1.88 (9H, m), 2.07-2.40 (5H, m), 2.30 (3H, s), 2.51 (2H, dt, J=7.3 and 2.6Hz), 2.91 (1H, dd, J=13.2 and 6.2Hz), 3.20 (1H, dd, J=13.2 and 9.9Hz), 3.24-3.33 (1H, m), 3.81-3.91 (1H, m), 4.14-4.24 (1H, m), 4.18 (1H, q, J=6.6Hz), 4.64-4.70 (1H, m), 5.16 (1H, dt, J=9.9 and 6.2Hz), 5.84 (1H, s), 7.05-7.15 (5H, m), 7.33-7.48 (6H, m), 7.55 (1H, d, J=9.9Hz), 7.59-7.67 (4H, m);
MASS (ES+): m/e 795.52 (M+1).

Example 79

Compound E79 was obtained in a manner similar to Example 6. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (3H, t, J=7.3Hz), 1.20-1.41 (6H, m), 1.28 (3H, s), 1.38 (3H, d, J=7.0Hz), 1.52-1.89 (4H, m), 2.07-2.40 (4H, m), 2.30 (3H, s), 2.46 (2H, dt, J=12.1 and 7.3Hz), 2.91 (1H, dd, J=13.7 and 6.2Hz), 3.20 (1H, dd, J=13.7 and 9.9Hz), 3.25-3.32 (1H, m), 3.55 (1H, d, J=4.8Hz), 3.81-3.91 (1H, m), 4.14-4.28 (2H, m), 4.64-4.70 (1H, m), 5.16 (1H, dt, J=9.9 and 6.2Hz), 5.85 (1H, s), 7.05-7.15 (5H, m), 7.53 (1H, d, J=9.9Hz);
MASS (ES+): m/e 557.41 (M+1).

Example 80

Compound E80 was obtained in a manner similar to Example 1. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (3H, t, J=7.2Hz), 1.09 (9H, s), 1.22 (3H, d, J=6.9Hz), 1.29 (3H, s), 1.38-1.51 (1H, m), 1.56-1.71 (1H, m), 1.73-2.43 (H, m), 3.13 (1H, dd, J=15.0 and 5.7Hz), 3.52 (1H, dd, J=15.0

and 9.9Hz), 3.73-3.84 (1H, m), 3.87-3.98 (1H, m), 4.17-4.26 (1H, m), 4.27 (1H, q, J=6.9Hz), 4.68 (1H, dd, J=7.5 and 2.4Hz), 5.57 (1H, dt, J=9.9 and 5.7Hz), 5.87 (1H, s), 6.60 (1H, d, J=15.6Hz), 6.86 (1H, dt, J=15.6 and 6.3Hz), 7.08-7.14 (1H, m), 7.15-7.21 (2H, m), 7.30-7.52 (6H, m), 7.55-7.68 (6H, m), 8.43-8.48 (1H, m);
MASS (ES+): m/e 780.56 (M+1).

Example 81

Compound E81 was obtained in a manner similar to Example 4. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.80 (3H, t, J=7.2Hz), 1.10 (9H, s), 1.18 (3H, d, J=6.6Hz), 1.20-2.46 (14H, m), 1.26 (3H, s), 2.46-2.57 (2H, m), 3.18-3.32 (1H, m), 3.58-3.97 (3H, m), 4.14-4.26 (2H, m), 4.66-4.73 (1H, m), 5.53-5.63 (1H, m), 5.90 (1H, s), 7.04-7.14 (1H, m), 7.28-7.48 (8H, m), 7.54-7.86 (6H, m), 8.50-8.58 (1H, m);
MASS (ES+): m/e 782.57 (M+1).

Example 82

Compound E82 was obtained in a manner similar to Example 6. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.87 (3H, t, J=7.2Hz), 1.17-1.96 (12H, m), 1.29 (3H, s), 1.38 (3H, d, J=6.9Hz), 2.06-2.57 (4H, m), 3.11-3.24 (1H, m), 3.12 (1H, dd, J=15.0 and 5.7Hz), 3.52 (1H, dd, J=15.0 and 10.2Hz), 3.74-3.84 (1H, m), 3.88-3.98 (1H, m), 4.14-4.28 (2H, m), 4.68 (1H, dd, J=7.5 and 2.4Hz), 5.58 (1H, dt, J=10.2 and 5.7 Hz), 5.92 (1H, s), 7.07-7.12 (1H, m), 7.14-7.20 (2H, m), 7.42-7.52 (1H, m), 7.57 (1H, dt, J=7.5 and 1.8Hz), 8.42-8.47 (1H, s);
MASS (ES+): m/e 544.49 (M+1).

Example 83

Compound E83 was obtained in a manner similar to Example 1. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.85 (3H, t, J=7.5Hz), 1.09 (9H, s), 1.14 (3H, d, J=7.3Hz), 1.29 (3H, s), 1.34-1.91 (6H, m), 2.00-2.40 (6H, m), 2.16 (3H, s), 2.92 (1H, dd, J=13.7 and 6.0Hz), 3.14-3.34 (2H, m), 3.78-3.94 (1H, m), 4.16-4.33 (2H, m), 4.67 (1H, br.d, J=6.0Hz), 5.08-5.24 (1H, m), 5.90 (1H, br.s), 6.61 (1H, br.d, J=15.8Hz), 6.80-6.94 (1H, m), 7.05-7.24 (4H, m), 7.30-7.48 (7H, m), 7.50-7.71 (6H, m);
MASS (ES+): m/e 836.37 (M+1).

Example 84

Compound E84 was obtained in a manner similar to Example 4. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (3H, t, J=7.3Hz), 1.10 (9H, s), 1.13-1.88 (10H, m), 1.21 (3H, d, J=6.8Hz), 1.28 (3H, s), 2.07-2.22 (2H, m), 2.16 (3H, s), 2.24-2.39 (2H, m), 2.44-2.56 (2H, m), 2.84-2.97 (1H, m), 3.12-3.34 (2H, m), 3.77-3.94 (1H, m), 4.10-4.34 (2H, m), 4.66 (1H,

br.d, J=6.6Hz), 5.07-5.21 (1H, m), 5.88 (1H, br.s), 7.06 (1H, d, J=10.6Hz), 7.13 (1H, s), 7.18 (2H, d, J=8.1Hz), 7.31-7.50 (7H, m), 7.53-7.71 (6H, m);
MASS (ES+): m/e 838.48 (M+1).

Example 85

Compound E85 was obtained in a manner similar to Example 6.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.85 (3H, t, J=7.3Hz), 1.21-1.91 (10H, m), 1.29 (3H, s), 1.39 (3H, d, J=7.3Hz), 2.08-2.24 (2H, m), 2.17 (3H, s), 2.26-2.40 (2H, m), 2.41-2.58 (2H, m), 2.91 (1H, dd, J=13.6 and 5.5Hz), 3.14-3.34 (2H, m), 3.51-3.61 (1H, m), 3.75-3.92 (1H, m), 4.13-4.30 (2H, m), 4.67 (1H, br.d, J=6.2Hz), 5.08-5.22 (1H, m), 5.90 (1H, s), 7.10 (1H, d, J=9.9Hz), 7.16 (1H, s), 7.19 (2H, d, J=8.6Hz), 7.40 (2H, d, J=8.6Hz), 7.56 (1H, d, J=9.2Hz);
MASS (ES+): m/e 600.42 (M+1).

Example 86

Compound E86 was obtained in a manner similar to Example 1.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.77 (3H, t, J=7.3Hz), 1.09 (9H, s), 1.19-2.35 (14H, m), 1.22 (3H, d, J=6.6Hz), 1.27 (3H, s), 2.93 (1H, dt, J=13.2 and 2.9Hz), 3.04 (1H, dd, J=13.9 and 7.7Hz), 3.21 (1H, dd, J=13.9 and 7.9Hz), 4.00 (1H, br.d, J=12.5Hz), 4.17-4.28 (1H, m), 4.27 (1H, q, J=6.6Hz), 4.98-5.08 (1H, m), 5.36 (1H, dt, J=10.6 and 7.9Hz), 5.95 (1H, s), 6.49 (1H, d, J=10.3Hz), 6.62 (1H, d, J=15.8Hz), 6.85 (1H, dt, J=15.8 and 7.0Hz), 7.15-7.48 (11H, m), 7.51 (1H, d, J=10.6Hz), 7.55-7.70 (4H, m);
MASS (ES+): m/e 793.52 (M+1).

Example 87

Compound E87 was obtained in a manner similar to Example 4.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.77 (3H, t, J=7.3Hz), 1.03-1.65 (9H, m), 1.10 (9H, s), 1.18 (3H, d, J=7.0Hz), 1.27 (3H, s), 1.68-1.84 (2H, m), 1.91-2.34 (5H, m), 2.51 (2H, dt, J=7.2 and 1.8Hz), 2.94 (1H, dt, J=13.6 and 2.9Hz), 3.04 (1H, dd, J=13.9, 7.1Hz), 3.21 (1H, dd, J=13.9 and 7.7Hz), 3.99 (1H, br.d, J=12.8Hz), 4.13-4.26 (2H, m), 4.98-5.07 (1H, m), 5.36 (1H, dt, J=10.3 and 7.5Hz), 5.93 (1H, s), 6.45 (1H, d, J=10.3Hz), 7.15-7.31 (5H, m), 7.32-7.49 (6H, m), 7.54 (1H, d, J=10.3Hz), 7.58-7.71 (4H, m);
MASS (ES+): m/e 795.53 (M+1).

Example 88

Compound E88 was obtained in a manner similar to Example 6.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.77 (3H, t, J=7.3Hz), 1.17-1.43 (4H, m),

1.27 (3H, s), 1.38 (3H, d, J=7.0Hz), 1.45-1.69 (6H, m), 1.70-1.86 (1H, m), 1.90-2.17 (4H, m), 2.19-2.34 (1H, m), 2.35-2.58 (2H, m), 2.93 (1H, dt, J=13.2 and 2.6Hz), 3.03 (1H, dd, J=13.9 and 7.3Hz), 3.21 (1H, dd, J=13.9 and 7.7Hz), 3.58 (1H, d, J=4.8Hz), 3.99 (1H, br.d, J=12.8Hz), 4.15-4.30 (2H, m), 5.00-5.06 (1H, m), 5.36 (1H, dt, J=10.3 and 7.5Hz), 6.02 (1H, s), 6.50 (1H, d, J=10.3Hz), 7.15-7.33 (5H, m), 7.53 (1H, d, J=10.3Hz);

MASS (ES+): m/e 557.39 (M+1).

Example 89

Compound E89 was obtained in a manner similar to Example 6. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.77 (3H, t, J=7.3Hz), 1.18-2.38 (14H, m), 1.28 (3H, s), 1.38 (3H, d, J=7.3Hz), 2.92 (1H, dt, J=13.2 and 2.6Hz), 3.04 (1H, dd, J=13.9 and 7.3Hz), 3.21 (1H, dd, J=13.9 and 7.7Hz), 3.66 (1H, d, J=5.1Hz), 3.95-4.06 (1H, m), 4.17-4.31 (1H, m), 4.39-4.51 (1H, m), 5.03 (1H, br.d, J=5.5Hz), 5.36 (1H, dt, J=10.3 and 7.7Hz), 5.99 (1H, s), 6.24 (1H, d, J=15.8Hz), 6.53 (1H, d, J=10.3Hz), 7.00 (1H, dt, J=15.8 and 7.0Hz), 7.15-7.35 (5H, m), 7.48 (1H, d, J=10.3Hz);

MASS (ES+): m/e 555.40 (M+1).

Example 90

Compound E90 was obtained in a manner similar to Example 1. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.83 (3H, t, J=7.3Hz), 1.10 (9H, s), 1.21 (3H, d, J=7.0Hz), 1.28 (3H, s), 1.38-2.42 (12H, m), 2.90-2.99 (1H, m), 2.99 (3H, s), 3.20 (1H, dd, J=13.6 and 8.8Hz), 3.26-3.36 (1H, m), 3.79-3.92 (1H, m), 4.17-4.32 (2H, m), 4.68 (1H, br.d, J=8.1Hz), 5.10-5.21 (1H, m), 5.85 (1H, s), 6.42 (1H, s), 6.62 (1H, br.d, J=15.6Hz), 6.87 (1H, dt, J=15.6 and 6.6Hz), 7.07 (1H, d, J=10.3Hz), 7.13 (2H, d, J=8.4Hz), 7.23 (2H, d, J=8.4Hz), 7.31-7.69 (10H, m);

MASS (ES-) m/e 870.56 (M-1).

Example 91

Compound E91 was obtained in a manner similar to Example 4. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.82 (3H, t, J=7.3Hz), 1.10 (9H, s), 1.21 (3H, d, J=7.0Hz), 1.28 (3H, s), 1.37-1.66 (7H, m), 1.71-1.91 (3H, m), 2.07-2.39 (4H, m), 2.51 (2H, dt, J=7.0 and 2.2Hz), 2.95 (1H, dd, J=13.6 and 6.6Hz), 2.99 (3H, s), 3.20 (1H, dd, J=13.6 and 9.2Hz), 3.26-3.36 (1H, m), 3.79-3.91 (1H, m), 4.14-4.24 (1H, m), 4.25 (1H, q, J=7.0Hz), 4.69 (1H, br.d, J=7.0Hz), 5.09-5.21 (1H, m), 5.90 (1H, s), 6.46 (1H, s), 7.03 (1H, d, J=9.9Hz), 7.12 (2H, d, J=8.4Hz), 7.23 (2H, d, J=8.4Hz), 7.32-7.50 (6H, m), 7.57-7.70 (5H, m);

MASS (ES-) m/e 872.46 (M-1).

Example 92

Compound E92 was obtained in a manner similar to Example 6. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.83 (3H, t, J=7.3Hz), 1.21-1.41 (4H, m), 1.29 (3H, s), 1.38 (3H, d, J=7.0Hz), 1.51-1.69 (3H, m), 1.70-1.90 (3H, m), 2.08-2.58 (6H, m), 2.95 (1H, dd, J=13.9 and 7.0Hz), 2.99 (3H, s), 3.20 (1H, dd, J=13.9 and 9.5Hz), 3.26-3.37 (1H, m), 3.55 (1H, br.d, J=4.0Hz), 3.79-3.91 (1H, m), 4.15-4.29 (2H, m), 4.69 (1H, br.d, J=7.3Hz), 5.15 (1H, dt, J=9.6 and 6.6Hz), 5.94 (1H, s), 6.56 (1H, s), 7.06 (1H, d, J=10.3Hz), 7.13 (2H, d, J=8.4Hz), 7.22 (2H, d, J=8.4Hz), 7.60 (2H, d, J=10.3Hz);

MASS (ES+): m/e 636.51 (M+1).

Example 93

Compound E93 was obtained in a manner similar to Example 1. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (3H, t, J=7.3Hz), 1.10 (9H, s), 1.23 (3H, d, J=6.6Hz), 1.30 (3H, s), 1.36-1.93 (6H, m), 2.08-2.41 (6H, m), 3.02 (1H, dd, J=13.5 and 6.2Hz), 3.22-3.38 (2H, m), 3.82-3.96 (1H, m), 4.15-4.28 (1H, m), 4.27 (1H, q, J=6.6Hz), 4.69 (1H, br.d, J=6.0Hz), 5.17-5.30 (1H, m), 5.85 (1H, s), 6.62 (1H, d, J=15.3Hz), 6.87 (1H, dt, J=15.3 and 7.0Hz), 7.13 (1H, d, J=10.3Hz), 7.27-7.48 (11H, m), 7.49-7.69 (9H, m);

MASS (ES+): m/e 855.61 (M+1).

Example 94

Compound E94 was obtained in a manner similar to Example 4. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (3H, t, J=7.4Hz), 1.10 (9H, s), 1.19 (3H, d, J=6.9Hz), 1.20-1.34 (7H, m), 1.29 (3H, s), 1.39-1.60 (3H, m), 1.69-1.90 (3H, m), 2.08-2.40 (4H, m), 2.52 (2H, dt, J=7.3 and 2.2Hz), 3.02 (1H, dd, J=13.5 and 6.3Hz), 3.20-3.38 (2H, m), 3.82-3.94 (1H, m), 4.12-4.26 (2H, m), 4.69 (1H, br.d, J=5.7Hz), 5.15-5.29 (1H, m), 5.84 (1H, s), 7.07 (1H, d, J=10.3Hz), 7.27-7.47 (12H, m), 7.48-7.69 (8H, m);

MASS (ES+): m/e 857.66 (M+1).

Example 95

Compound E95 was obtained in a manner similar to Example 6. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (3H, t, J=7.5Hz), 1.21-1.41 (4H, m), 1.27 (3H, s), 1.38 (3H, d, J=7.0Hz), 1.53-1.70 (3H, m), 1.71-1.90 (3H, m), 2.08-2.58 (6H, m), 3.01 (1H, dd, J=13.9 and 6.1Hz), 3.21-3.38 (2H, m), 3.56 (1H, d, J=4.7Hz), 3.82-3.94 (1H, m), 4.14-4.30 (2H, m), 4.69 (1H, br.d, J=5.7Hz), 5.16-5.29 (1H, m), 5.87 (1H, s), 7.11 (1H, d, J=10.0Hz), 7.23-7.36 (3H, m), 7.38-7.46 (2H, m), 7.47-7.64 (5H, m);

MASS (ES+): m/e 619.55 (M+1).

Example 96

Compound E96 was obtained in a manner similar to Example 1. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (3H, t, J=7.3Hz), 1.09 (3x3H, s), 1.22 (3H, d, J=7Hz), 1.29 (3H, s), 1.45 (2H, m), 1.58-1.91 (4H, m), 2.07-2.40 (6H, m), 2.90 (1H, dd, J=13.5 and 6Hz), 3.19 (1H, dd, J=13.5 and 10Hz), 3.26 (1H, m), 3.85 (2x3H, s), 3.86 (1H, m), 4.21 (1H, m), 4.27 (1H, q, J=7Hz), 4.67 (1H, m), 5.16 (1H, ddd, J=10, 10 and 6Hz), 5.90 (1H, s), 6.62 (1H, d, J=15.5Hz), 6.74-6.80 (3H, m), 6.86 (1H, dt, J=15.5 and 7Hz), 7.14 (1H, d, J=10Hz), 7.30-7.48 (6H, m), 7.54 (1H, d, J=10Hz), 7.57-7.68 (5H, m);

MASS (ES+): m/e 839.

Example 97

Compound E97 was obtained in a manner similar to Example 4. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (3H, t, J=7.3Hz), 1.10 (3x3H, s), 1.18 (3H, d, J=6.5Hz), 1.18-1.32 (4H, m), 1.29 (3H, s), 1.45 (2H, m), 1.58-1.69 (1H, m), 1.70-1.89 (3H, m), 2.08-2.40 (4H, m), 2.51 (2H, m), 2.90 (1H, dd, J=13.5 and 6Hz), 3.20 (1H, dd, J=13.5 and 10Hz), 3.26 (1H, m), 3.85 (2x3H, s), 3.85 (1H, m), 4.14-4.25 (2H, m), 4.67 (1H, m), 5.15 (1H, ddd, J=10, 10 and 6Hz), 5.89 (1H, s), 6.75-6.82 (3H, m), 7.09 (1H, d, J=10Hz), 7.32-7.50 (5H, m), 7.58 (1H, d, J=10Hz), 7.58-7.69 (4H, s);

MASS (ES-): m/e 876 (M+Cl).

Example 98

Compound E98 was obtained in a manner similar to Example 6. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.85 (3H, t, J=7.5Hz), 1.23-1.39 (4H, m), 1.29 (3x3H, s), 1.38 (3H, d, J=7Hz), 1.54-1.71 (3H, m), 1.72-1.90 (3H, m), 2.08-2.24 (2H, m), 2.25-2.57 (4H, m), 2.89 (1H, dd, J=13.5 and 6Hz), 3.19 (1H, dd, J=13.5 and 10Hz), 3.26 (1H, m), 3.55 (1H, d, J=4.5Hz), 3.85 (2x3H, s), 3.85 (1H, m), 4.14-4.29 (2H, m), 4.67 (1H, m), 5.15 (1H, ddd, J=10, 10 and 6Hz), 5.88 (1H, s), 6.74-6.79 (3H, m), 7.12 (1H, d, J=10Hz), 7.55 (1H, d, J=10Hz);

MASS (ES-): m/e 601;

$[\alpha]_D^{24}$= -104.6° (c=0.32, $CHCl_3$).

Example 99

Compound E99 was obtained in a manner similar to Example 1. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.87 (3H, d, J=7Hz), 0.88 (3H, t, J=7Hz), 0.91 (3H, t, J=7Hz), 1.09 (3x3H, s), 1.12-1.24 (2H, m), 1.22 (3H, d, J=6.5Hz), 1.30 (3H, s), 1.38-1.52 (2H, m), 1.54-1.71 (1H, m), 1.74-2.10

(4H, m), 2.14-2.43 (6H, m), 3.53 (1H, m), 3.90 (1H, m), 4.21 (1H, m), 4.27 (1H, q, J=6.5Hz), 4.59 (1H, dd, J=10.5 and 10.5Hz), 4.77 (1H, m), 5.87 (1H, s), 6.61 (1H, d, J=15 and 5Hz), 6.86 (1H, dt, J=15.5 and 7Hz), 7.19 (1H, d, J=10Hz), 7.30-7.49 (7H, m), 7.56-7.69 (4H, m);
MASS (ES-) m/e 743.

Example 100

Compound E100 was obtained in a manner similar to Example 4.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.86 (3H, d, J=7Hz), 0.88 (3H, t, J=7Hz), 0.91 (3H, t, J=7Hz), 1.10 (3x3H, s), 1.16-1.28 (3H, m), 1.18 (3H, d, J=6.5Hz), 1.30 (3H, s), 1.37-1.70 (4H, m), 1.72-2.10 (4H, m), 2.11-2.43 (4H, m), 2.50 (2H, m), 3.53 (1H, dt, J=10, 7.5Hz), 3.88 (1H, ddd, J=10, 10 and 5Hz), 4.18 (1H, m), 4.18 (1H, q, J=6.5Hz), 4.58 (1H, dd, J=10.5 and 10.5Hz), 4.75 (1H, m), 5.88 (1H, s), 7.13 (1H, d, J=10Hz), 7.32-7.48 (7H, m), 7.57-7.70 (4H, m);
MASS (ES-) m/e 745.

Example 101

Compound E101 was obtained in a manner similar to Example 6.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.86 (3H, d, J=7Hz), 0.88 (3H, t, J=7Hz), 0.91 (3H, t, J=7Hz), 1.06-1.40 (5H, m), 1.30 (3H, s), 1.38 (3H, d, J=6.5Hz), 1.50-2.10 (8H, m), 2.12-2.58 (6H, m), 3.53 (1H, dt, J=10 and 7.5Hz), 3.56 (1H, d, J=4.5Hz), 3.89 (1H, ddd, J=10, 10 and 5Hz), 4.14-4.29 (2H, m), 4.58 (1H, dd, J=10.5 and 10.5Hz), 4.76 (1H, dd, J=8 and 1.5Hz), 5.91 (1H, s), 7.17 (1H, d, J=10.5Hz), 7.38 (1H, d, J=10.5Hz);
MASS (ES-) m/e 507;
$[\alpha]_D^{24}$= -133.3° (c=0.25, $CHCl_3$).

Example 102

Compound E102 was obtained in a manner similar to Example 1.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (3H, d, J=6.6Hz), 0.86 (3H, t, J=7.3Hz), 1.09 (3H, s), 1.22 (3H, d, J=6.6Hz), 1.32-2.02 (9H, m), 2.09-2.46 (4H, m), 2.78 (1H, dd, J=14.5 and 8Hz), 3.16 (1H, dd, J=14.5 and 8Hz), 3.51 (1H, m), 3.76 (3H, s), 4.03 (1H, m), 4.26 (1H, m), 4.27 (1H, q, J=6.6Hz), 4.48 (1H, dd, J=10.5 and 10.5Hz), 4.69 (1H, m), 4.72 (1H, m), 6.28 (1H, d, J=10.5Hz), 6.29 (1H, d, J=10Hz), 6.58 (1H, d, J=15.5Hz), 6.80 (2x1H, d, J=8.5Hz), 6.83 (1H, dt, J=15 and 5.7Hz), 7.11 (2x1H, d, J=8.5Hz), 7.22 (1H, d, J=10.5Hz), 7.30-7.48 (6H, m), 7.55-7.69 (4H, m);
MASS (ES-) m/e 821.

Example 103

Compound E103 was obtained in a manner similar to Example 4.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (3H, d, J=6.6Hz), 0.86 (3H, d, J=7.3Hz), 1.10 (3x3H, s), 1.13-2.02 (13H, m), 1.18 (3H, d, J=6.5Hz), 2.25-2.52 (4H, m), 2.78 (1H, dd, J=14.2 and 7.7Hz), 3.15 (1H, dd, J=14.2 and 7.7Hz), 3.51 (1H, m), 3.76 (3H, s), 4.02 (1H, m), 4.18 (3H, q, J=6.5Hz), 4.22 (1H, m), 4.48 (1H, dd, J=10.6 and 10.5Hz), 4.68 (1H, ddd, J=9.7, 7.7 and 7.7Hz), 4.72 (1H, m), 6.29 (1H, d, J=9.7Hz), 6.30 (1H, d, J=10.5Hz), 6.80 (2x1H, d, J=8.8Hz), 7.11 (2x1H, d, J=8.8Hz), 7.16 (1H, d, J=10.7Hz), 7.31-7.48 (6H, m), 7.57-7.67 (4H, m);
MASS (ES-) m/e 823.

Example 104

Compound E104 was obtained in a manner similar to Example 6.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (3H, d, J=6.6Hz), 0.86 (3H, t, J=7.4Hz), 1.09 (1H, m), 1.18-1.32 (4H, m), 1.37 (3H, d, J=6.8Hz), 1.49-2.03 (8H, m), 2.26-2.55 (4H, m), 2.79 (1H, dd, J=14.5 and 7.9Hz), 3.15 (1H, dd, J=14.5 and 7.7Hz), 3.51 (1H, m), 3.57 (1H, d, J=4.5Hz), 3.77 (3H, s), 4.02 (1H, m), 4.17-4.29 (2H, m), 4.48 (1H, dd, J=10.7 and 10.6Hz), 4.68 (1H, m), 4.73 (1H, m), 6.30 (2x1H, br-d, J=10Hz), 6.81 (2x1H, d, J=8.5Hz), 7.12 (2x1H, d, J=8.5Hz), 7.20 (1H, d, J=10.6Hz);
MASS (ES-) m/e 585;
$[\alpha]_D^{30}$= -61.5° (c=0.33, $CHCl_3$)

Example 105

Compound E105 was obtained in a manner similar to Example 1.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.09 (3x3H, s), 1.24 (3H, d, J=7Hz), 1.43 (2H, m), 1.61-1.89 (4H, m), 2.10-2.40 (4H, m), 2.77 (1H, dd, J=14 and 7Hz), 2.87 (1H, dd, J=13.5, 5Hz), 3.08 (1H, m), 3.16 (1H, dd, J=14 and 8Hz), 3.18 (1H, dd, J=13.5 and 11Hz), 3.77 (3H, s), 3.94 (1H, m), 4.27 (1H, m), 4.27 (1H, q, J=7Hz), 4.61 (1H, dd, J=8 and 2.5Hz), 4.69 (1H, ddd, J=10, 8 and 7Hz), 5.16 (1H, ddd, J=11, 10 and 5Hz), 6.30 (1H, d, J=10Hz), 6.59 (1H, br-d, J=16Hz), 6.81 (2x1H, d, J=8.5Hz), 6.84 (1H, dt, J=16 and 7Hz), 7.12 (2x1H, d, J=8.5Hz), 7.12-7.48 (14H, m), 7.56-7.69 (4H, m);
MASS (ES-) m/e 855.

Example 106

Compound E106 was obtained in a manner similar to Example 4.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.10 (3x3H, s), 1.14-1.30 (4H, m), 1.18 (3H, d, J=7Hz), 1.36-1.82 (6H, m), 2.10-2.40 (2H, m), 2.49 (2H, m), 2.77 (1H, dd, J=14.5 and 7Hz), 2.87 (1H, dd, J=13 and 5.5Hz), 3.02-3.24 (3H, m), 3.77 (3H, s), 3.94 (1H, m), 4.18 (1H, q, J=7Hz), 4.24 (1H, m), 4.61 (1H, m), 4.69 (1H, m), 5.06 (1H, ddd, J=10, 10 and 5.5Hz),

6.29 (1H, d, J=9.5Hz), 6.46 (1H, d), 6.81 (2x1H, d, J=9Hz), 7.09-7.30 (8H, m), 7.32-7.48 (6H, m), 7.58-7.68 (4H, m);
MASS (ES-) m/e 857.

Example 107

Compound E107 was obtained in a manner similar to Example 6. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.20-1.36 (4H, m), 1.38 (3H, d, J=7Hz), 1.54-1.88 (6H, m), 2.12-2.56 (4H, m), 2.78 (1H, dd, J=14.5 and 7Hz), 2.87 (1H, dd, J=13.5 and 5.5Hz), 3.02-3.24 (3H, m), 3.56 (1H, d, J=5Hz), 3.94 (1H, m), 4.17-4.30 (2H, m), 4.61 (1H, m), 4.68 (1H, m), 5.06 (1H, ddd, J=10, 10 and 5.5Hz), 6.32 (1H, d, J=10Hz), 6.46 (1H, d, J=10Hz), 6.82 (2x1H, d, J=8.5Hz), 7.08-7.32 (8H, m);
MASS (ES-) m/e 619;
$[\alpha]_D^{30}$= -60.9° (C=0.31, $CHCl_3$).

Example 108

Compound E108 was obtained in a manner similar to Example 1. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.91 (3H, t, J=7.5Hz), 1.09 (3H, s), 1.22 (3H, d, J=7Hz), 1.36 (3H, s), 1.46 (2H, m), 1.56-1.72 (1H, m), 1.78-2.04 (3H, m), 2.12-2.54 (6H, m), 3.74 (1H, m), 4.04 (1H, m), 4.21-4.32 (2H, m), 4.75 (1H, m), 5.98 (1H, s), 6.19 (1H, d, J=10Hz), 6.61 (1H, br-d, J=16Hz), 6.86 (1H, dt, J=16 and 7Hz), 7.16 (1H, d, J=10Hz), 7.24-7.49 (11H, m), 7.56-7.68 (4H, m), 8.08 (1H, d, J=10Hz);
MASS (ES-) m/e 763.

Example 109

Compound E109 was obtained in a manner similar to Example 4. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.91 (3H, t, J=7.3Hz), 1.10 (3x3H, s), 1.18 (3H, d, J=7Hz), 1.18-1.30 (4H, m), 1.36 (3H, s), 1.38-2.06 (6H, m), 2.09-2.58 (6H, m), 3.74 (1H, m), 4.03 (1H, m), 4.18 (1H, q, J=7Hz), 4.26 (1H, m), 4.75 (1H, dd, J=8, 2Hz), 5.98 (1H, s), 6.18 (1H, d, J=10Hz), 7.10 (1H, d, J=10.5Hz), 7.28-7.49 (11H, m), 7.58-7.69 (4H, m), 8.12 (1H, d, J=10Hz);
MASS (ES-) m/e 765.

Example 110

Compound E110 was obtained in a manner similar to Example 6. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.92 (3H, t, J=7.3Hz), 1.24-1.40 (4H, m), 1.36 (3H, s), 1.38 (3H, d, J=7Hz), 1.53-1.68 (2H, m), 1.73-2.57 (10H, m), 3.55 (1H, d, J=5Hz), 3.74 (1H, m), 4.04 (1H, m), 4.17-4.30 (2H, m), 4.76 (1H, dd, J=8.2Hz), 5.99 (1H, s), 6.19 (1H, d, J=10.3Hz), 7.14 (1H, d, J=10.6Hz), 7.25-7.42 (5H, m), 8.10 (1H, d, J=10.3Hz);
MASS (ES-) m/e 527;

$[\alpha]_D^{30}$= -174.4° (c=0.22, $CHCl_3$).

Example 111

Compound E111 was obtained in a manner similar to Example 1. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.87 (3H, t, J=7.5Hz), 0.96 (2H, m), 1.09 (3x3H, s), 1.12-1.32 (2H, m), 1.22 (3H, d, J=7Hz), 1.29 (3H, s), 1.36-1.51 (2H, m), 1.54-2.00 (13H, m), 2.10-2.44 (6H, m), 3.52 (1H, dt, J=10 and 7Hz), 3.96 (1H, m), 4.21 (1H, dt, J=10, 7.5Hz), 4.26 (1H, q, J=7Hz), 4.74 (1H, dt, J=8 and 2Hz), 5.00 (1H, d, J=10 and 8Hz), 5.85 (1H, s), 6.81 (1H, d, J=16Hz), 6.86 (1H, dt, J=16 and 7Hz), 7.14 (1H, d, J=10Hz), 7.30-7.50 (7H, m), 7.56-7.69 (4H, m);
MASS (ES-) m/e 783.

Example 112

Compound E112 was obtained in a manner similar to Example 4. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.86 (3H, t, J=7.3Hz), 0.96 (2H, m), 1.10 (3x3H, s), 1.13-1.34 (6H, m), 1.18 (3H, d, J=6.5Hz), 1.29 (3H, s), 1.45 (2H, m), 1.52-2.00 (13H, m), 2.08-2.43 (4H, m), 2.50 (2H, m), 3.52 (1H, dt, J=10.5 and 7Hz), 3.96 (1H, m), 4.18 (1H, m), 4.18 (1H, q, J=6.5Hz), 4.74 (1H, dd, J=8 and 2Hz), 5.00 (1H, dd, J=10 and 7.5Hz), 5.85 (1H, s), 7.09 (1H, d, J=10Hz), 7.31-7.48 (7H, m), 7.57-7.67 (4H, m);
MASS (ES-) m/e 785.

Example 113

Compound E113 was obtained in a manner similar to Example 6. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.87 (3H, t, J=7.3Hz), 0.96 (2H, m), 1.08-1.40 (8H, m), 1.29 (3H, s), 1.38 (3H, d, J=7.2Hz), 1.50-2.00 (13H, m), 2.08-2.57 (6H, m), 3.52 (1H, ddd, J=10, 7.5 and 7Hz), 3.56 (1H, d, J=5Hz), 3.96 (1H, m), 4.13-4.28 (2H, m), 4.74 (1H, dd, J=8 and 2Hz), 4.99 (1H, dt, J=10 and 8Hz), 5.88 (1H, s), 7.12 (1H, d, J=10Hz), 7.34 (1H, d, J=10Hz);
MASS (ES-) m/e 547.

Example 114

Compound E114 was obtained in a manner similar to Example 1. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.80 (3H, t, J=7.3Hz), 0.86 (3H, t, J=7.3Hz), 0.96 (2H, m), 1.10 (3x3H, m), 1.17 (2H, m), 1.42 (2H, m), 1.52-2.00 (15H, m), 2.10-2.44 (6H, m), 3.52 (1H, dt, J=10 and 7Hz), 3.96 (1H, m), 4.15 (1H, t, J=6Hz), 4.20 (1H, dt, J=10.5 and 7.5Hz), 4.74 (1H, dd, J=8 and 2Hz), 5.00 (1H, dt, J=10 and 8Hz), 5.85 (1H, s), 6.54 (1H, br-d, J=16Hz), 6.79 (1H, dt, J=16, 7Hz), 7.14 (1H, d, J=10.5Hz), 7.28-7.48 (7H, m), 7.54-7.68 (4H, m);

MASS (ES-) m/e 797.

Example 115

Compound E115 was obtained in a manner similar to Example 4. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.81 (3H, t, J=7.5Hz), 0.86 (3H, t, J=7.3Hz), 0.96 (2H, m), 1.11 (3x3H, s), 1.12-1.27 (6H, m), 1.29 (3H, s), 1.37 (2H, m), 1.47-1.98 (15H, m), 2.07-2.49 (6H, m), 3.52 (1H, dt, J=10 and 7Hz), 3.95 (1H, m), 4.10 (1H, t, J=7Hz), 4.16 (1H, dt, J=10 and 7Hz), 4.73 (1H, dd, J=8 and 2Hz), 4.99 (1H, dt, J=10 and 7Hz), 5.84 (1H, s), 7.08 (1H, d, J=10Hz), 7.32-7.48 (7H, m), 7.58-7.66 (4H, m);
MASS (ES+): m/e 799.

Example 116

Compound E116 was obtained in a manner similar to Example 6. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.87 (3H, t, J=7.3Hz), 0.94 (3H, t, J=7Hz), 0.94 (2H, m), 1.08-1.40 (8H, m), 1.29 (3H, s), 1.50-2.00 (15H, m), 2.07-2.50 (6H, m), 3.49 (1H, d, J=4.5Hz), 3.52 (1H, m), 3.96 (1H, m), 4.10-4.25 (2H, m), 4.74 (1H, dd, J=7.5 and 2Hz), 4.99 (1H, dt, J=10 and 7.5Hz), 5.88 (1H, s), 7.12 (1H, d, J=10Hz), 7.34 (1H, d, J=10Hz);
MASS (ES-) m/e 561.

Example 117

Compound E117 was obtained in a manner similar to Example 1. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.09 (3x3H, s), 1.22 (3H, d, J=7Hz), 1.24-1.92 (14H, m), 1.96-2.39 (5H, m), 2.62 (1H, m), 2.95 (1H, dd, J=13.5 and 6Hz), 3.21 (1H, m), 3.25 (1H, dd, J=13.5 and 10Hz), 3.93 (1H, m), 4.22 (1H, m), 4.27 (1H, q, J=7Hz), 4.66 (1H, m), 5.16 (1H, ddd, J=10, 10 and 6Hz), 5.74 (1H, s), 6.62 (1H, d, J=16Hz), 6.87 (1H, dt, J=16 and 7Hz), 7.15-7.29 (6H, m), 7.29-7.48 (7H, m), 7.56-7.68 (4H, m);
MASS (ES-) m/e 804.

Example 118

Compound E118 was obtained in a manner similar to Example 4. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.10 (3x3H, s), 1.18 (3H, d, J=7Hz), 1.20-1.68 (14H, m), 1.69-1.92 (4H, m), 2.04 (1H, m), 2.18 (1H, m), 2.32 (1H, m), 2.51 (2H, m), 2.63 (1H, m), 2.95 (1H, dd, J=14 and 6Hz), 3.21 (1H, m), 3.25 (1H, dd, J=14 and 10Hz), 3.92 (1H, m), 4.18 (1H, q, J=7Hz), 4.20 (1H, m), 4.66 (1H, m), 5.16 (1H, ddd, J=10, 10 and 6Hz), 5.73 (1H, s), 7.13 (1H, s), 7.17-7.31 (5H, m), 7.33-7.48 (7H, m), 7.59-7.68 (4H, m);
MASS (ES-) m/e 805.

Example 119

Compound E119 was obtained in a manner similar to Example 6.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 1.20-1.92 (19H, m), 1.94-2.70 (5H, m), 2.95 (1H, dd, J=13.5, 6Hz), 3.20 (1H, m), 3.24 (1H, dd, J=13.5 and 10Hz), 3.56 (1H, d, J=4.5Hz), 3.92 (1H, m), 4.15-4.29 (2H, m), 4.64 (1H, m), 5.16 (1H, ddd, J=10, 10 and 6Hz), 5.75 (1H, s), 7.17 (1H, d, J=10Hz), 7.19-7.32 (5H, m), 7.38 (1H, d, J=10Hz);

MASS (ES-) m/e 567;

$[\alpha]_D^{25}$ = -98.8° (c=0.33, $CHCl_3$).

Example 120

Compound E120 was obtained in a manner similar to Example 1.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.81 (3H, t, J=7.5Hz), 1.11 (3x3H, s), 1.23-1.93 (16H, m), 1.96-2.37 (5H, m), 2.64 (1H, m), 2.96 (1H, dd, J=13 and 6Hz), 3.15-3.31 (2H, m), 3.93 (1H, m), 4.16 (1H, t, J=6Hz), 4.22 (1H, m), 4.66 (1H, m), 5.17 (1H, m), 5.72 (1H, s), 6.56 (1H, d, J=16Hz), 6.81 (1H, dt, J=16 and 7Hz), 7.15-7.48 (13H, m), 7.55-7.69 (4H, m);

MASS (ES+): m/e 819.

Example 121

Compound E121 was obtained in a manner similar to Example 4.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.81 (3H, t, J=7.3Hz), 1.11 (3x3H, s), 1.14-1.90 (20H, m), 1.95-2.23 (2H, m), 2.26-2.49 (3H, m), 2.64 (1H, m), 2.95 (1H, dd, J=13.5 and 6Hz), 3.21 (1H, m), 3.25 (1H, dd, J=13.5 and 10Hz), 3.91 (1H, m), 4.11 (1H, t, J=6Hz), 4.18 (1H, m), 4.66 (1H, m), 5.16 (1H, ddd, J=10, 10 and 6Hz), 5.69 (1H, s), 7.12 (1H, d, J=10Hz), 7.16-7.31 (5H, m), 7.32-7.48 (7H, m), 7.57-7.67 (4H, m);

MASS (ES+): m/e 819.

Example 122

Compound E122 was obtained in a manner similar to Example 6.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.94 (3H, t, J=7.4Hz), 1.20-1.95 (20H, m), 2.03 (1H, m), 2.16 (1H, m), 2.31 (1H, m), 2.44 (2H, m), 2.62 (1H, m), 2.95 (1H, dd, J=14 and 6Hz), 3.14-3.30 (2H, m), 3.49 (1H, d, J=5Hz), 3.92 (1H, m), 4.08-4.26 (2H, m), 4.68 (1H, m), 5.16 (1H, ddd, J=10, 10 and 6Hz), 5.72 (1H, s), 7.12-7.31 (5H, m), 7.16 (1H, d, J=10Hz), 7.38 (1H, d, J=10Hz);

MASS (ES-) m/e 581;

$[\alpha]_D^{25}$= -100.4° (c=0.30, $CHCl_3$).

Example 123

Compound E123 was obtained in a manner similar to Example 1.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.90 (2H, m), 1.06-1.32 (4H, m), 1.10 (9H, s), 1.23 (3H, d, J=7Hz), 1.36-1.52 (3H, m), 1.56-1.82 (10H, m), 2.14-2.39

(4H, m), 2.94 (1H, dd, J=14 and 5Hz), 3.10 (1H, m), 3.23 (1H, dd, J=14 and 10Hz), 3.94 (1H, m), 4.27 (1H, m), 4.27 (1H, q, J=7Hz), 4.52 (1H, m), 4.62 (1H, m), 5.09 (1H, ddd, J=10, 10 and 5Hz), 6.04 (1H, d, J=10Hz), 6.48 (1H, d, J=10Hz), 6.61 (1H, d, J=16Hz), 6.87 (1H, dt, J=16 and 7Hz), 7.16-7.50 (12H, m), 7.57-7.70 (4H, m);
MASS (ES+): m/e 855.

Example 124

Compound E124 was obtained in a manner similar to Example 4.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.92 (2H, m), 1.08-1.32 (8H, m), 1.10 (9H, s), 1.19 (3H, d, J=7Hz), 1.38-1.50 (3H, m), 1.58-1.84 (10H, m), 2.19 (2H, m), 2.32 (2H, m), 2.51 (2H, br-t, J=7Hz), 2.94 (1H, dd, J=13 and 5Hz), 3.10 (1H, m), 3.23 (1H, dd, J=13 and 10Hz), 3.93 (1H, m), 4.18 (1H, q, J=7Hz), 4.25 (1H, dt, J=10 and 7Hz), 4.52 (1H, dt, J=11 and 8Hz), 4.62 (1H, m), 5.09 (1H, ddd, J=10, 10 and 5Hz), 6.06 (1H, d, J=10Hz), 6.51 (1H, d, J=11Hz), 7.13 (1H, d, J=10Hz), 7.18-7.32 (5H, m), 7.34-7.48 (6H, m), 7.59-7.67 (4H, m);
MASS (ES-) m/e 833.

Example 125

Compound E125 was obtained in a manner similar to Example 6.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.92 (1H, m), 1.07-1.50 (10H, m), 1.38 (3H, d, J=7Hz), 1.54-1.90 (11H, m), 2.18 (1H, m), 2.33 (1H, m), 2.46 (2H, m), 2.93 (1H, dd, J=13 and 5Hz), 3.10 (1H, m), 3.22 (1H, dd, J=13, 10Hz), 3.56 (1H, d, J=5Hz), 3.93 (1H, m), 4.18-4.31 (2H, m), 4.52 (1H, dt, J=10 and 7Hz), 4.62 (1H, m), 5.08 (1H, ddd, J=10, 10 and 5Hz), 6.08 (1H, d, J=10Hz), 6.49 (1H, d, J=10Hz), 7.16 (1H, d, J=10Hz), 7.17-7.32 (5H, m);
MASS (ES-) m/e 595;
$[\alpha]_D^{23}$ = -53.8° (c=0.09, $CHCl_3$).

Example 126

Compound E126 was obtained in a manner similar to Example 1.
^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.80 (3H, t, J=7Hz), 0.90 (2H, m), 1.04-1.32 (4H, m), 1.10 (9H, s), 1.36-1.50 (3H, m), 1.52-1.90 (12H, m), 2.10-2.36 (4H, m), 2.96 (1H, dd, J=13 and 5Hz), 3.10 (1H, m), 3.22 (1H, dd, J=13 and 10Hz), 3.93 (1H, m), 4.15 (1H, t, J=6Hz), 4.27 (1H, ddd, J=10, 8 and 7Hz), 4.52 (1H, ddd, J=10, 8 and 7Hz), 4.62 (1H, m), 5.09 (1H, ddd, J=10, 10 and 5Hz), 6.05 (1H, d, J=10Hz), 6.48 (1H, d, J=10Hz), 6.53 (1H, d, J=16Hz), 6.79 (1H, dt, J=16 and 7Hz), 7.14-7.47 (12H, m), 7.54-7.68 (4H, m);
MASS (ES-) m/e 845.

Example 127

Compound E127 was obtained in a manner similar to Example 4. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.81 (3H, t, J=7Hz), 0.90 (2H, m), 1.11 (9H, s), 1.12-1.82 (23H, m), 2.15-2.47 (4H, m), 2.94 (1H, dd, J=13 and 5Hz), 3.10 (1H, m), 3.22 (1H, dd, J=13 and 10Hz), 3.93 (1H, m), 4.11 (1H, t, J=6Hz), 4.24 (1H, dt, J=10 and 7Hz), 4.52 (1H, dt, J=10 and 7Hz), 4.62 (1H, m), 5.09 (1H, ddd, J=10, 10 and 5Hz), 6.06 (1H, d, J=10Hz), 6.51 (1H, d, J=10Hz), 7.12 (1H, d, J=10Hz), 7.18-7.32 (5H, m), 7.33-7.47 (6H, m), 7.58-7.66 (4H, m);
MASS (ES-) m/e 847.

Example 128

Compound E128 was obtained in a manner similar to Example 6. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.80-1.00 (2H, m), 0.94 (3H, t, J=7Hz), 1.06-1.96 (23H, m), 2.18 (1H, m), 2.31 (1H, m), 2.44 (2H, m), 2.93 (1H, dd, J=13 and 5Hz), 3.09 (1H, m), 3.22 (1H, dd, J=13 and 10Hz), 3.51 (1H, d, J=5Hz), 3.93 (1H, m), 4.15 (1H, m), 4.26 (1H, dt, J=10 and 8Hz), 4.52 (1H, dt, J=10 and 7Hz), 4.62 (1H, m), 5.08 (1H, ddd, J=10, 10 and 5Hz), 6.08 (1H, d, J=10Hz), 6.50 (1H, d, J=10Hz), 7.16 (1H, d, J=10Hz), 7.16-7.33 (5H, m);
MASS (ES-) m/e 609;
$[\alpha]_D^{23} = -49.6°$ (c=0.26, $CHCl_3$).

Example 129

Compound E129 was obtained in a manner similar to Example 1. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.90 (2H, m), 1.09 (9H, s), 1.11-1.33 (8H, m), 1.22 (3H, d, J=7Hz), 1.36-1.52 (3H, m), 1.59-1.90 (6H, m), 2.14-2.38 (4H, m), 2.94 (1H, dd, J=13 and 5Hz), 3.10 (1H, m), 3.22 (1H, dd, J=13 and 6Hz), 3.94 (1H, m), 4.22-4.33 (2H, m), 4.52 (1H, dt, J=8 and 7Hz), 4.62 (1H, m), 5.09 (1H, ddd, J=10, 6 and 5Hz), 6.04 (1H, d, J=10Hz), 6.48 (1H, d, J=10Hz), 6.60 (1H, d, J=16Hz), 6.86 (1H, dt, J=16 and 7Hz), 7.15-7.48 (12H, m);
MASS (ES+): m/e 833.

Example 130

Compound E130 was obtained in a manner similar to Example 4. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.89 (2H, m), 1.05-1.34 (8H, m), 1.10 (9H, s), 1.18 (3H, d, J=7Hz), 1.37-1.52 (3H, m), 1.58-1.85 (10H, m), 2.12-2.38 (2H, m), 2.50 (2H, m), 2.93 (1H, dd, J=13 and 5Hz), 3.10 (1H, m), 3.22 (1H, dd, J=13 and 11Hz), 3.93 (1H, m), 4.18 (1H, q, J=7Hz), 4.24 (1H, dt, J=10 and 8Hz), 4.52 (1H, dt, J=10 and 7Hz), 4.62 (1H, m), 5.08 (1H, ddd, J=11, 10 and 5Hz), 6.06 (1H, d, J=10Hz), 6.50 (1H, d, J=10Hz),

7.12 (1H, d, J=10Hz), 7.17-7.32 (5H, m), 7.33-7.48 (6H, m), 7.58-7.67 (4H, m);
MASS (ES-) m/e 833.

Example 131

Compound E131 was obtained in a manner similar to Example 6. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.90 (2H, m), 1.06-1.90 (21H, m), 1.38 (3H, d, J=7Hz), 2.18 (1H, m), 2.27-2.58 (3H, m), 2.93 (1H, dd, J=13 and 5Hz), 3.10 (1H, m), 3.22 (1H, dd, J=13 and 10Hz), 3.58 (1H, br-d, J=3Hz), 3.93 (1H, m), 4.18-4.32 (2H, m), 4.52 (1H, dt, J=10 and 8Hz), 4.62 (1H, m), 5.08 (1H, ddd, J=10, 10 and 5Hz), 6.12 (1H, d, J=10Hz), 6.51 (1H, d, J=10Hz), 7.13-7.33 (6H, m);
MASS (ES-) m/e 595;
$[\alpha]_D^{23}$ = -46.4° (c=1.39, $CHCl_3$).

Example 132

Compound E132 was obtained in a manner similar to Example 1. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.80 (3H, t, J=7.5Hz), 0.87 (3H, t, J=7.5Hz), 1.10 (9H, s), 1.29 (3H, s), 1.42 (2H, m), 1.54-1.69 (3H, m), 1.74-1.92 (3H, m), 1.98-2.42 (8H, m), 2.65 (1H, m), 3.32 (1H, m), 3.75 (1H, m), 4.15 (1H, t, J=6Hz), 4.21 (1H, m), 4.72 (1H, m), 4.85 (1H, m), 5.83 (1H, s), 6.54 (1H, d, J=16Hz), 6.80 (1H, dt, J=16 and 7Hz), 7.11 (1H, d, J=10Hz), 7.15-7.23 (3H, m), 7.25-7.47 (9H, m), 7.55-7.67 (4H, m);
MASS (ES+): m/e 829.

Example 133

Compound E133 was obtained in a manner similar to Example 4. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.81 (3H, t, J=7.5Hz), 0.87 (3H, t, J=7.3Hz), 1.11 (9H, s), 1.14-1.25 (4H, m), 1.28 (3H, s), 1.37 (2H, m), 1.48-1.92 (6H, m), 2.00-2.25 (4H, m), 2.26-2.49 (4H, m), 2.64 (2H, m), 3.32 (1H, m), 3.76 (1H, m), 4.10 (1H, t, J=6Hz), 4.17 (1H, dt, J=10, 7Hz), 4.72 (1H, m), 4.84 (1H, dt, J=10 and 7Hz), 5.82 (1H, s), 7.05 (1H, d, J=10Hz), 7.14-7.22 (3H, m), 7.24-7.48 (9H, m), 7.57-7.66 (4H, m);
MASS (ES-) m/e 807.

Example 134

Compound E134 was obtained in a manner similar to Example 6. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.88 (3H, t, J=7Hz), 0.94 (3H, t, J=7Hz), 1.22-1.40 (4H, m), 1.29 (3H, s), 1.52-1.70 (4H, m), 1.74-1.98 (4H, m), 2.01-2.26 (4H, m), 2.29-2.50 (4H, m), 2.65 (2H, m), 3.33 (1H, m), 3.50 (1H, d, J=5Hz), 3.75 (1H, m), 4.08-4.26 (2H, m), 4.73 (1H, m), 4.85 (1H, ddd, J=10, 8 and 7Hz), 5.84 (1H, s), 7.09 (1H, d, J=10Hz), 7.15-7.24 (3H, m), 7.25-7.33 (2H, m), 7.42 (1H, d, J=10Hz);

MASS (ES-) m/e 569.

Example 135

Compound E135 was obtained in a manner similar to Example 1. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.87 (3H, t, J=7.5Hz), 1.09 (9H, s), 1.21 (3H, d, J=7Hz), 1.29 (3H, s), 1.45 (2H, m), 1.64 (1H, m), 1.75-1.92 (3H, m), 2.00-2.42 (8H, m), 2.65 (2H, m), 3.32 (1H, m), 3.75 (1H, m), 4.21 (1H, m), 4.27 (1H, q, J=7Hz), 4.72 (1H, m), 4.85 (1H, dt, J=10 and 7.5Hz), 5.83 (1H, s), 6.61 (1H, d, J=16Hz), 6.86 (1H, dt, J=16 and 7Hz), 7.11 (1H, d, J=10Hz), 7.15-7.23 (3H, m), 7.24-7.49 (9H, m), 7.56-7.69 (4H, m);

MASS (ES+) m/e 815.

Example 136

Compound E136 was obtained in a manner similar to Example 4. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.87 (3H, t, J=7Hz), 1.10 (9H, s), 1.18 (3H, d, J=7Hz), 1.20-1.32 (4H, m), 1.28 (3H, s), 1.38-1.52 (3H, m), 1.72-1.91 (3H, m), 2.00-2.42 (6H, m), 2.50 (2H, m), 2.64 (2H, m), 3.34 (1H, m), 3.74 (1H, m), 4.18 (1H, q, J=7Hz), 4.18 (1H, m), 4.72 (1H, m), 4.84 (1H, m), 5.83 (1H, s), 7.05 (1H, d, J=10Hz), 7.14-7.22 (3H, m), 7.24-7.32 (2H, m), 7.33-7.49 (7H, m), 7.58-7.67 (4H, m);

MASS (ES-) m/e 793.

Example 137

Compound E137 was obtained in a manner similar to Example 6. ^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.87 (3H, t, J=7.5Hz), 1.20-1.40 (4H, m), 1.29 (3H, s), 1.38 (3H, d, J=7Hz), 1.53-1.69 (3H, m), 1.75-1.92 (3H, m), 1.98-2.25 (4H, m), 2.26-2.55 (4H, m), 2.64 (2H, m), 3.32 (1H, m), 3.56 (1H, d, J=4.5Hz), 3.74 (1H, m), 4.10-4.29 (2H, m), 4.72 (1H, m), 4.84 (1H, ddd, J=10, 7.5 and 7.5Hz), 5.84 (1H, s), 7.08 (1H, d, J=10Hz), 7.12-7.23 (3H, m), 7.24-7.33 (2H, m), 7.42 (1H, d, J=10Hz);

MASS (ES-) m/e 555.

Example 138

Compound E138 was obtained in a manner similar to the method disclosed in WO00/21979.

Example 139

To a stirred solution of Compound E138 (506 mg) in methanol (10 ml) was added aqueous sodium periodate (1.08 M, 2ml) at ambient temperature and the resulting mixture was stirred at the same temperature overnight. The solvent was removed under reduced pressure and the residue was dissolved in ethyl acetate and 1N hydrochloric acid. The organic layer was separated, washed with brine, dried over sodium sulfate,

filtered and evaporated under reduced pressure. The crude product was purified by flash chromatography eluting with 5% methanol/chloroform (v/v) as a solvent mixture to give the Compound E139 (480 mg) as a white amorphous solid.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (3H, t, J=7.5Hz), 0.88 (3H, d, J=6.5Hz), 1.20-1.42 (5H, m), 1.28 (3H, s), 1.53-1.70 (3H, m), 1,81 (1H, m), 2.17 (1H, m), 2.24-2.42 (4H, m), 2.62 (1H, m), 2.73 (1H, dd, J=9.5 and 8Hz), 2.96 (1H, dd, J=13.5 and 6Hz), 3.23 (1H, dd, J=13.5 and 10Hz), 4.05 (1H, dd, J=9.5 and 7.5Hz), 4.23 (1H, m), 4.69 (1H, dd, J=8.2Hz), 5.16 (1H, ddd, J=10, 10 and 6Hz), 6.10 (1H, s), 7.16-7.32 (6H, m), 7.6 0(1H, d, J=10Hz);

MASS (ES+): m/e 529.

Example 140

To a stirred solution of Compound E138 (1000 mg) in methanol (20 ml) was added aqueous solution of sodium periodate (1.08 M, 2 ml) at ambient temperature and the resulting mixture was stirred at the same temperature overnight. The solvent was concentrated in vacuo and the residue was dissolved in ethyl acetate and added 1 N hydrochloric acid. The organic layer was separated, washed with brine, dried over sodium sulfate, filtered and evaporated under reduced pressure. The crude product was purified by flash chromatography using 5% methanol/chloroform (v/v) as a solvent mixture to give the Compound E140 (949 mg) as a white amorphous solid.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (3H, t, J=7.5Hz), 0.87 (3H, d, J=7Hz), 1.21-1.45 (5H, m), 1.28 (3H, s), 1.53-1.70 (3H, m), 1.82 (1H, m), 2.17 (1H, m), 2.25-2.42 (4H, m), 2.62 (1H, m), 2.72 (1H, dd, J=9 and 8Hz), 2.96 (1H, dd, J=13 and 6Hz), 3.23 (1H, dd, J=13 and 10Hz), 4.05 (1H, dd, J=9 and 7Hz), 4.22 (1H, m), 4.68 (1H, dd, J=7 and 2Hz), 5.15 (1H, ddd, J=10, 9 and 6 Hz), 6.04 (1H, s), 7.15-7.32 (6H, m), 7.58 (1H, d, J=9Hz);

MASS (ES+): m/e 529.

Example 141

To a stirred solution of Compound E140 in dichloromethane (2 ml) was aded N-methylhydroxylamine hydrochloride (18 mg), 1-hydroxybenzotriazole (58.2 mg) and a solution of 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide (67.0 mg) in dichloromethane at ambient temperature and the resulting mixture was stirred at the same temperature for three days. This mixture was poured into water and the organic layer was separated. The organic layer was

washed with brine, dried over sodium sulfate, filtered and evaporated under reduced pressure. The residue was purified by flash chromatography using 9% methanol/chloroform (v/v) as a solvent mixture to give the Compound E141 (18 mg) as a white amorphous solid.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (3H, t, J=7.5Hz), 0.88 (3H, d, J=6.5Hz), 1.20-1.44 (5H, m), 1.28 (3H, s), 1.52-1.90 (5H, m), 2.15 (1H, m), 2.25-2.42 (3H, m), 2.62 (1H, m), 2.73 (1H, dd, J=9.5 and 7.5Hz), 2.82 (1H, s), 2.96 (1H, dd, J=13.5 and 6Hz), 3.24 (1H, dd, J=13.5 and 10Hz), 4.06 (1H, dd, J=9.5 and 8Hz), 4.19 (1H, dt, J=10 and 7.5Hz), 4.67 (1H, dd, J=8 and 2Hz), 5.16 (1H, ddd, J=10, 10 and 6Hz), 5.83 (1H, s), 7.16 (1H, d, J=10Hz), 7.19-7.33 (5H, m), 7.54 (1H, d, J=10Hz);

MASS (ES-) m/e 556;

$[\alpha]_D^{21}$ = -130.8° (c=0.30, $CHCl_3$).

Example 142

To a stirred solution of Compound E139 (473 mg) in dichloromethane (5 ml) was added 1-hydroxybenzotriazole (181 mg), a solution of 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide (208 mg) in chloroform and N,O-dimethylhydroxylamine hydrochloric acid (131 mg) at ambient temperature and the resulting mixture was left at the same temperature for two weeks. This mixture was poured into 10% aqueous solution of citric acid and the organic layer was separated, washed with saturated sodium hydrogen carbonate and brine. The organic phase was dried over sodium sulfate, filtered and evaporated under reduced pressure. The residue was purified by flash chromatography eluting with ethyl acetate as an eluting solvent to give the Compound E142 (453 mg) as a white amorphous solid.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (3H, t, J=7.5Hz), 0.88 (3H, d, J=6.6Hz), 1.25-1.44 (6H, m), 1.29 (3H, s), 1.55-1.69 (2H, m), 1.83 (1H, m), 2.14 (1H, m), 2.26-2.45 (4H, m), 2.65 (1H, m), 2.73 (1H, dd, J=9.5 and 8Hz), 2.96 (1H, dd, J=13.5 and 6Hz), 3.18 (3H, s), 3.24 (1H, dd, J=13.5 and 10Hz), 3.68 (3H, s), 4.06 (1H, dd, J=9.5 and 7.3Hz), 4.21 (1H, m), 4.67 (1H, dd, J=8 and 2Hz), 5.16 (1H, ddd, J=10.3, 10 and 6Hz), 5.81 (1H, s), 7.14 (1H, d, J=10.2Hz), 7.16-7.32 (5H, m), 7.56 (1H, d, J=10.3Hz);

MASS (ES+): m/e 572.

Example 143

To a stirred solution of the Compound E142 (97 mg) in tetrahydrofuran (4 ml) was added ethyl magnesium bromide (1.04 M in tetrahydrofuran, 1.6 ml) dropwise at -78°C and the mixture was allowed

to warm to 0°C. The reaction mixture was quenched with saturated sodium hydrogen carbonate at ambient temperature and the resulting mixture was extracted with ethyl acetate. The organic layer was washed with brine, dried over sodium sulfate, filtered and evaporated under reduced pressure. The residue was purified by preparative thin layer chromatography using 90% ethyl acetate/hexane (v/v) as a solvent mixture to give the Compound E143 (38 mg) as a white amorphous solid.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (3H, 7, J=7.3Hz), 0.88 (3H, d, J=6.6Hz), 1.05 (3H, t, J=7.3Hz), 1.20-1.44 (6H, m), 1.28 (3H, s), 1.48-1.71 (3H, m), 1.81 (1H, m), 2.14 (1H, m), 2.26-2.46 (5H, m), 2.63 (1H, m), 2.73 (1H, dd, J=9.5 and 8Hz), 2.96 (1H, dd, J=13.5 and 6Hz), 3.24 (1H, dd, J=13.5 and 10Hz), 4.06 (1H, dd, J=9.5 and 7.5Hz), 4.19 (1H, dt, J=10 and 7.5Hz), 4.67 (1H, dd, J=8 and 2Hz), 5.16 (1H, ddd, J=10 and 10.6Hz), 5.79 (1H, s), 7.14 (1H, d, J=10Hz), 7.18-7.32 (5H, m), 7.54 (1H, d, J=10Hz);

MASS (ES+): m/e 541.

Example 144

To a stirred solution of dimethyl 3-fluoro-2-oxopropylphosphonate (86.1 mg) in 2-propanol (3 ml) was added cesium carbonate (152 mg) at ambient temperature and the mixture was stirred at the same temperature for half an hour. To the resulting light yellow solution was added a solution of the starting compound (Compound (105)) (200 mg) in isopropyl alcohol at the same temperature and the mixture was stirred at the same temperature for two hours. The reaction mixture was quenched with 10% aqueous solution of citric acid, diluted with ethyl acetate and water. The organic layer was separated and washed with saturated sodium hydrogen carbonated and brine. The organic phase was dried over sodium sulfate, filtered and evaporated under reduced pressure. The residue was purified by preparative thin layer chromatography using 66% ethyl acetate/hexane (v/v) as a solvent mixture to give Compound E144 (68 mg) as a white amorphous solid.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.83 (3H, t, J=7Hz), 1.29 (3H, s), 1.50 (2H, m), 1.64-1.92 (4H, m), 2.08-2.40 (6H, m), 2.97 (1H, dd, J=13.5 and 6Hz), 3.24 (1H, dd, J=13.5 and 9.5Hz), 3.26 (1H, m), 3.85 (1H, m), 4.24 (1H, ddd, J=10, 7.5 and 7Hz), 4.67 (1H, m), 4.96 (2H, d, J=48Hz), 5.19 (1H, ddd, J=10.5, 9.5 and 6Hz), 5.82 (1H, s), 6.36 (1H, m), 7.00 (1H, ddd, J=16, 7 and 7Hz), 7.15 (1H, d, J=10Hz), 7.17-7.32 (5H, m), 7.50 (1H, d, J=10.5Hz);

MASS (ES-) m/e 527;

$[\alpha]_D^{23}$= -90.7 (c=0.25, $CHCl_3$).

Example 145

To a stirred solution of dimethyl 3-fluoro-2-oxopropylphosphonate (356 mg) in 2-propanol (10 ml) was added cesium carbonate (599 mg) at 0°C and the mixture was stirred at ambient temperature for half an hour. To the resulting yellow brown solution was added a solution of the starting compound (Compound (81)) (484 mg) in tetrahydrofuran (5 ml) and 2-propanol (5 ml) at the same temperature and the resulting mixture was stirred for half an hour at the same temperature. The reaction mixture was quenched with 10% aqueous solution of citric acid, diluted with ethyl acetate and water. The organic layer was separated and washed with water and brine. The organic phase was dried over sodium sulfate, filtered and evaporated under reduced pressure. The residue was purified by preparative thin layer chromatography using ethyl acetate to give the Compound E145 (320 mg) as a white amorphous solid.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.85 (3H, t, J=7.3Hz), 1.29 (3H, s), 1.40-1.90 (6H, m), 2.08-2.40 (6H, m), 2.89 (1H, dd, J=14 and 6Hz), 3.18 (1H, dd, J=14 and 10Hz), 3.26 (1H, m), 3.77 (3H, s), 3.86 (1H, m), 4.22 (1H, dt, J=10 and 7.5Hz), 4.67 (1H, m), 4.96 (2H, d, J=47Hz), 5.14 (1H, ddd, J=10, 10 and 6Hz), 5.93 (1H, s), 6.36 (1H, m), 6.81 (2x1H, d, J=8.5Hz), 7.00 (1H, dt, J=16 and 7Hz), 7.14 (2x1H, d, J=8.5Hz), 7.18 (1H, d, J=10Hz), 7.49 (1H, d, J=10Hz);

MASS (ES-) m/e 557;

$[\alpha]_D^{30}$= -108.6°(c=0.16, $CHCl_3$).

Example 146

Compound E146 was obtained in a manner similar to Example 4.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (3H, t, J=7Hz), 1.23-1.42 (4H, m), 1.28 (3H, s), 1.53-1.90 (6H, m), 2.07-2.24 (2H, m), 2.25-2.45 (2H, m), 2.54 (2H, m), 2.89 (1H, dd, J=13.5 and 6.5Hz), 3.18 (1H, dd, J=13.5 and 9.5Hz), 3.26 (1H, m), 3.77 (3H, s), 3.85 (1H, m), 4.19 (1H, dt, J=10.5 and 7.5Hz), 4.67 (1H, m), 4.79 (2H, d, J=48Hz), 5.13 (1H, ddd, J=10, 9.5 and 6.5Hz), 5.80 (1H, s), 6.81 (2x1H, d, J=8.5Hz), 7.10 (1H, d, J=10.5Hz), 7.14 (2x1H, d, J=8.5Hz), 7.53 (1H, d, J=10Hz);

MASS (ES-) m/e 559;

$[\alpha]_D^{30}$= -118.8° (c=0.40, $CHCl_3$).

Example 147

To a stirred solution of the starting compound E146 (55 mg) in

ethanol (4 ml) was added a solution of sodium borohydride in ethanol at 0°C and stirred at ambient temperature for half an hour. The reaction was quenched with water and most of the solvent was removed under reduced pressure. The residue was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate, filtered and evaporated under reduced pressure. The resiidue was purified by preparative thin layer chromatography using 50% ethyl acetate/hexane (v/v) as an eluting solvent mixture to give an amorphous, which was dissolved in tert-butyl alcohol and lyophilized to give Compound E147 (49 mg).

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (3H, t, J=7.3Hz), 1.22-1.53 (8H, m), 1.28 (3H, s), 1.56-1.90 (4H, m), 2.07-2.24 (3H, m), 2.25-2.40 (2H, m), 2.89 (1H, dd, J=14 and 6Hz), 3.18 (1H, dd, J=14 and 9.5Hz), 3.26 (1H, m), 3.77 (3H, s), 3.80-3.94 (2H, m), 4.20 (1H, m), 4.27 (1H, m), 4.41 (1H, ddd, J=47, 9.5 and 3Hz), 4.67 (1H, m), 5.13 (1H, ddd, J=10, 9.5 and 6Hz), 5.94 (1H, d, J=5Hz), 6.81 (2x1H, d, J=8.5Hz), 7.11 (1H, d, J=10Hz), 7.14 (2x1H, d, J=8.5Hz), 7.54 (1H, d, J=10Hz);

MASS (ES-): m/e 561;

$[\alpha]_D^{24}$= -107.5° (c=0.21, $CHCl_3$).

Example 148

To a stirred solution of Compound E138 (165 mg) in dichrolomethane (5 ml) was added a solution of diethylaminosulfurtrifluoride (71.7 mg) in dichloromethane at ambient temperature. The reaction mixture was stirred at the same temperature for three days. The solvent was removed under reduced pressure and the residue was dissolved in ethyl acetate. The organic layer was washed with saturated sodium hydrogen carbonate, water and brine. The organic phase was dried over sodium sulfate, filtered and evaporated under reduced pressure. The crude product was purified by preparative thin layer chromatography using 50% ethyl acetate/hexane (v/v) as a solvent mixture to give the Compound E148 (136 mg) as a white amorphous solid.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.84 (3H, t, J=7.3Hz), 0.88 (3H, d, J=6.5Hz), 1.22-1.44 (4H, m), 1.29 (3H, s), 1.47 (3H, dd, J=24 and 7Hz), 1.52-1.68 (3H, m), 1.82 (1H, m), 2.14 (1H, dq, J=14 and 7.3Hz), 2.26-2.43 (2H, m), 2.56-2.68 (3H, m), 2.72 (1H, dd, J=9.5 and 8Hz), 2.96 (1H, dd, J=13.5 and 6Hz), 3.24 (1H, dd, J=13.5 and 10Hz), 4.06 (1H, dd, J=9.5 and 7Hz), 4.20 (1H, dt, J=10 and 7.5Hz), 4.67 (1H, dd, J=8 and 2Hz), 4.86 (1H, dq, J=50 and 7Hz), 5.16 (1H, ddd, J=10, 10 and 6Hz), 5.84

(1H, s), 7.16 (1H, d, J=10Hz), 7.16-7.31 (5H, m), 7.54 (1H, d, J=10Hz); MASS (ES-): m/e 557;

$[\alpha]_D^{25}$= -100.4° (c=0.26, $CHCl_3$).

Example 149

To a stirred solution of the Compound E142 (99 mg) in tetrahydrofuran (4 ml) was added n-butyllithium (1.50 M in hexane, 0.60 ml) dropwise at -78°C. The mixture was stirred at the same temperature for twenty-five minutes. The reaction mixture was quenched with water at the same temperature and the resulting mixture was extracted with ethyl acetate. The organic layer was washed with brine, dried over sodium sulfate, filtered and evaporated under reduced pressure. The residue was purified by preparative thin layer chromatography using 50% ethyl acetate/hexane (v/v) as a solvent mixture to give Compound E149 (38 mg) as a white amorphous solid.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.80-0.96 (9H, m), 1.20-1.44 (6H, m), 1.29 (3H, s), 1.48-1.69 (5H, m), 1.81 (1H, m), 2.16 (1H, m), 2.26-2.42 (5H, m), 2.63 (1H, m), 2.72 (1H, m), 2.96 (1H, m), 3.25 (1H, m), 4.06 (1H, m), 4.19 (1H, m), 4.67 (1H, br-d, J=8Hz), 5.16 (1H, m), 5.79 (1H, s), 7.14 (1H, d, J=10Hz), 7.18-7.32 (5H, m), 7.54 (1H, d, J=10Hz); MASS (ES+): m/e 569;

$[\alpha]_D^{21}$= -116.2° (c=0.18, $CHCl_3$).

Example 150

A solution of Compound (289) (300 mg) in a mixture of piperidine (1.2 ml) and N,N-dimethylformamide (4.8 ml) was stirred at ambient temperature for three hours. The mixture was concentrated in vacuo and the residue was purified by flash chromatography using ethyl acetate as a solvent to afford the Compound E150 (275 mg) as a pale yellow oil.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.83 (3H, t, J=7.3Hz), 1.28 (3H, s), 1.34-1.98 (8H, m), 2.07-2.23 (2H, m), 2.24-2.42 (2H, m), 2.83 (1H, dd, J=13.6 and 5.9Hz), 3.13 (1H, dd, J=13.6 and 9.9Hz), 3.19-3.34 (1H, m), 3.62 (2H, br.s), 3.80-3.90 (1H, m), 4.18-4.29 (1H, m), 4.31 (2H, t, J=6.4Hz), 4.67 (1H, br.d, J=6.6Hz), 5.11 (1H, dt, J=10.1 and 5.9Hz), 5.90 (1H, s), 6.60 (2H, d, J=8.4Hz), 7.01 (2H, d, J=8.4Hz), 7.18 (1H, d, J=10.3Hz), 7.39-7.62 (4H, m), 7.99-8.06 (2H, m);

MASS (ES+): m/e 592.46 (M+1).

Example 151

To a stirred solution of the Compound E150 (540 mg) in pyridine (4 ml) was added methanesulfonyl chloride (110 mg) in an ice bath.

The resulting mixture was stirred at the same temperature for two hours. The mixture was concentrated in vacuo and the residue was extracted with ethyl acetate, washed with water, 5% (w/v) potassium hydrogen sulfate, saturated sodium bicarbonate and brine. The organic phase was dried over magnesium sulfate, filtered and concentrated in vacuo. The residue was purified by flash chromatography using ethyl acetate as a solvent to give the Compound E151 (538 mg) as a pale yellow amorphous solid.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.81 (3H, t, J=7.5Hz), 1.29 (3H, s), 1.35-2.00 (8H, m), 2.06-2.41 (4H, m), 2.96 (1H, dd, J=13.9 and 6.6Hz), 2.99 (3H, s), 3.21 (1H, dd, J=13.9 and 9.5Hz), 3.26-3.36 (1H, m), 3.79-3.92 (1H, m), 4.20-4.32 (1H, m), 4.32 (2H, t, J=6.4Hz), 4.70 (1H, br.d, J=7.3Hz), 5.09-5.22 (1H, m), 5.97 (1H, s), 6.51 (1H, s), 7.10 (1H, d, J=10.0Hz), 7.13 (2H, d, J=8.8Hz), 7.23 (2H, d, J=8.8Hz), 7.40-7.49 (2H, m), 7.52-7.66 (2H, m), 8.00-8.07 (2H, m);

MASS (ES+): m/e 670.53 (M+1).

Example 152

To a stirred solution of Compound E150 (260 mg) in pyridine (2 ml) was added acetic anhydride (1 ml) followed by a catalytic amount of 4-(dimethylamino)pyridine at ambient temperature and the resulting mixture was stirred at the same temperature for one hour. The volatiles were removed under reduced pressure and the residue was purified by flash chromatopraphy using ethyl acetate then 5% methanol/ethyl acetate (v/v) as a solvent mixture to give the Compound E153 (260 mg) as a pale yellow amorphous solid.

^{1}H-NMR (300MHz, $CDCl_3$, δ): 0.82 (3H, t, J=7.3Hz), 1.27 (3H, s), 1.36-1.98 (8H, m), 2.06-2.24 (2H, m), 2.16 (3H, s), 2.25-2.41 (2H, m), 2.91 (1H, dd, J=13.5 and 5.7Hz), 3.20 (1H, dd, J=13.5 and 9.9Hz), 3.21-3.34 (1H, m), 3.78-3.90 (1H, m), 4.18-4.30 (1H, m), 4.31 (2H, d, J=6.6Hz), 4.66 (1H, br.d, J=7.0Hz), 5.14 (1H, dt, J=9.9 and 5.9Hz), 5.89 (1H, s), 7.12 (1H, d, J=9.9Hz), 7.18 (2H, d, J=8.4Hz), 7.40 (2H, d, J=8.4Hz), 7.42-7.48 (2H, m), 7.50-7.60 (2H, m), 7.98-8.07 (2H, m);

MASS (ES+): m/e 634.73.

The compounds obtained in the above-mentioned Preparations and Examples are listed in the following Tables 2-1 to 2-55.

Table 2

Table 2-1

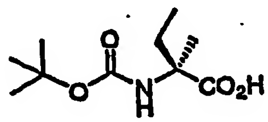
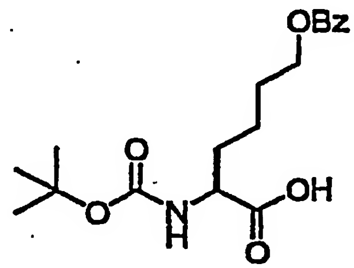
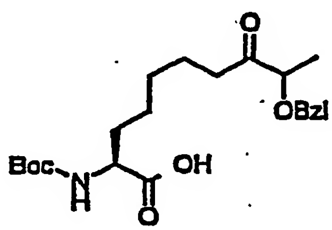
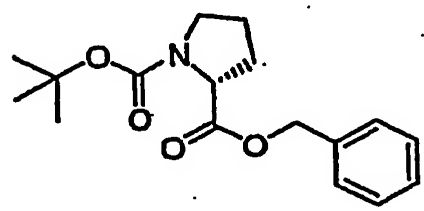
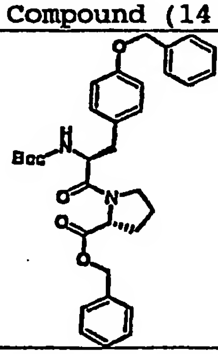
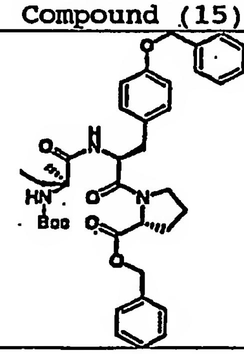
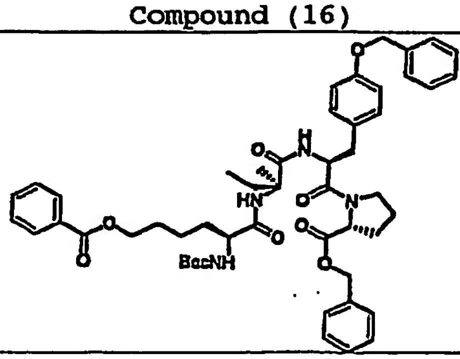
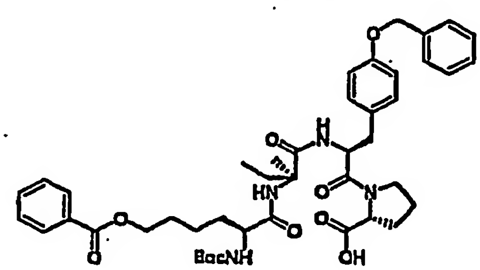
Compound (1)	Compound (5)
	
Compound (12)	Compound (13)
	
Compound (14)	Compound (15)
	
Compound (16)	Compound (17)
	

Table 2-2

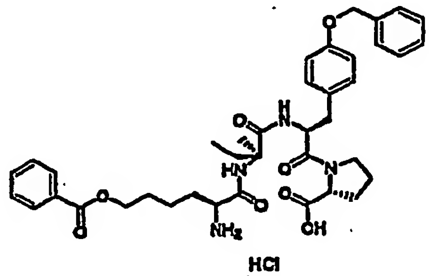
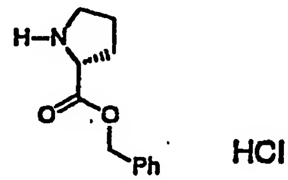
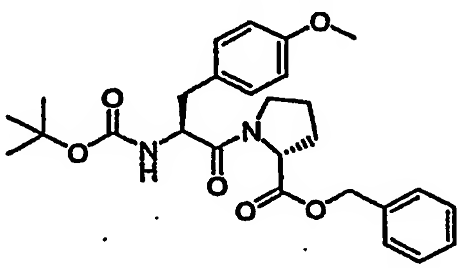
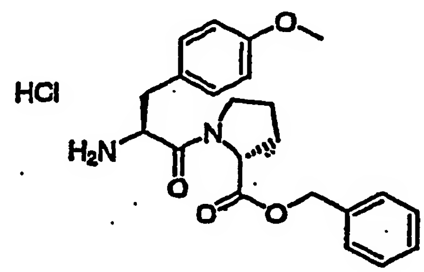
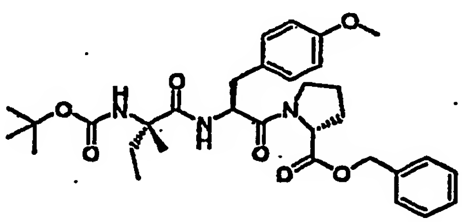
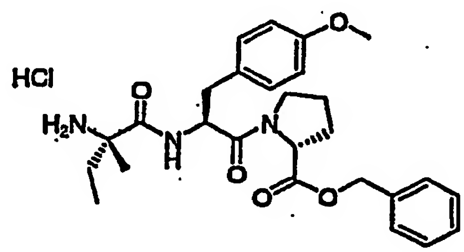
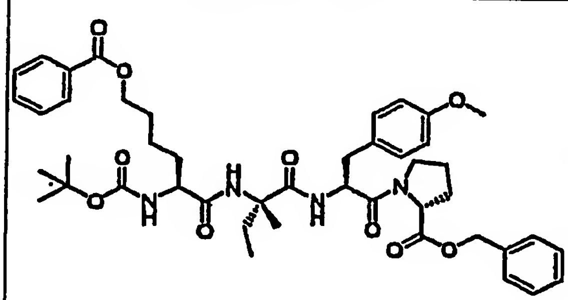
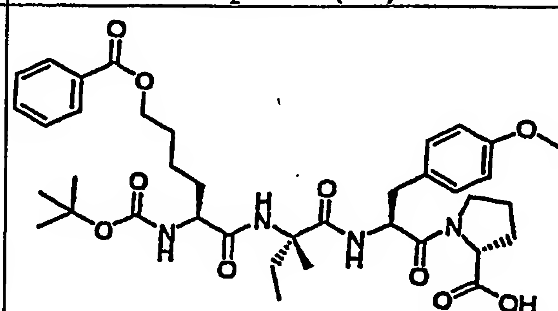
Compound (18)	Compound (19)
	
Compound (20)	**Compound (21)**
	
Compound (22)	**Compound (23)**
	
Compound (24)	**Compound (25)**
	

Table 2-3

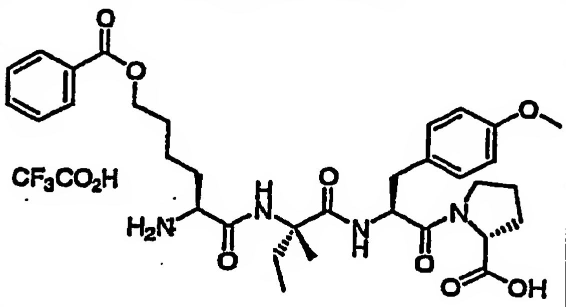
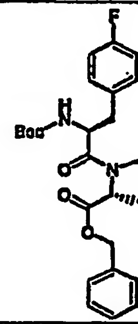
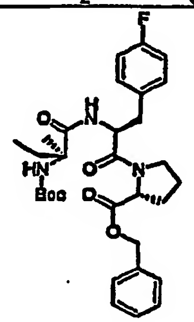
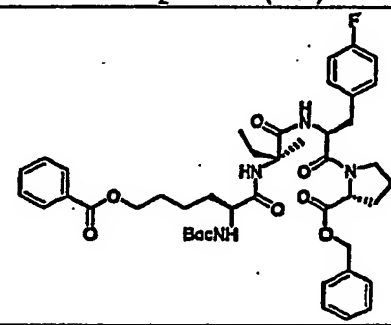
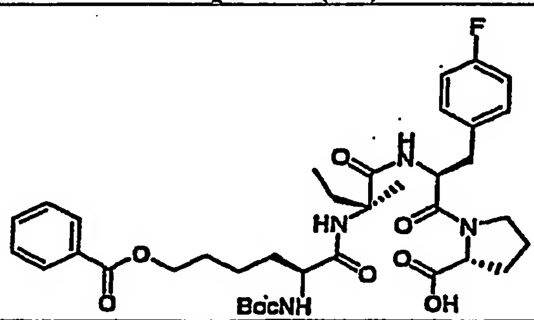
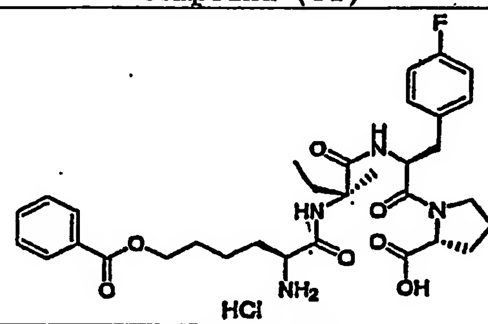
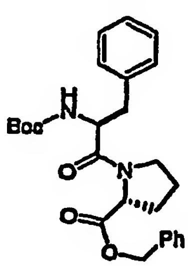
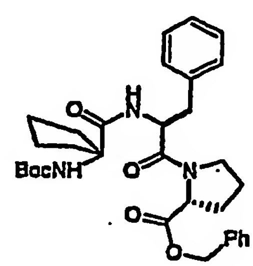
Compound (26)	Compound (27)
	
Compound (28)	Compound (29)
	
Compound (30)	Compound (31)
	
Compound (32)	Compound (33)
	

Table 2-4

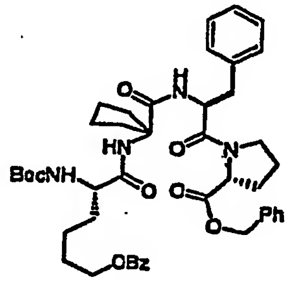
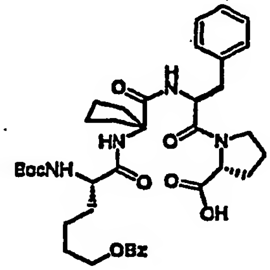
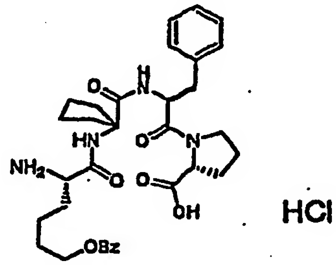
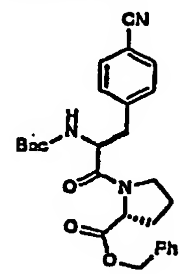
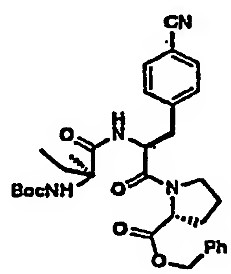
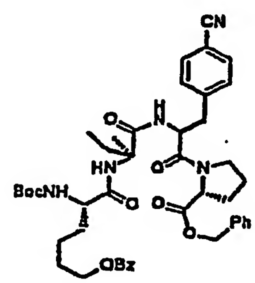
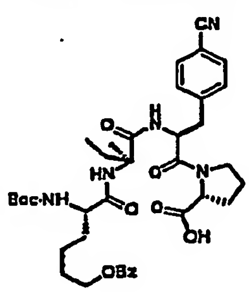
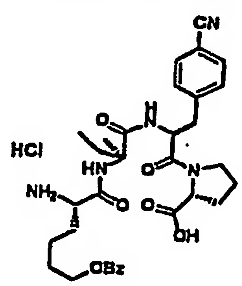
Compound (34)	Compound (35)
	
Compound (36)	**Compound (37)**
	
Compound (38)	**Compound (39)**
	
Compound (40)	**Compound (41)**
	

Table 2-5

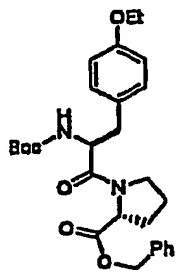
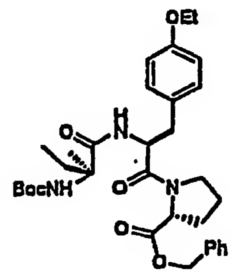
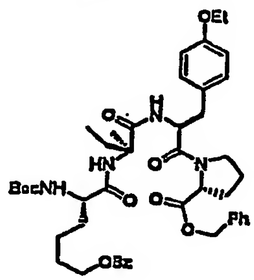
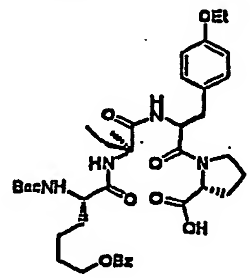
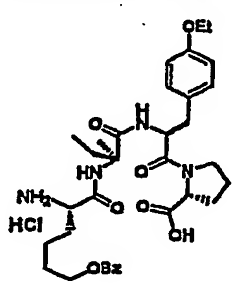
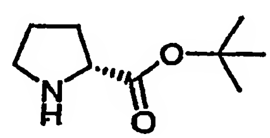
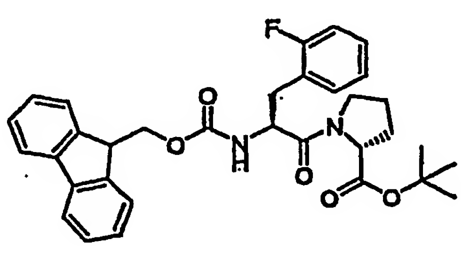
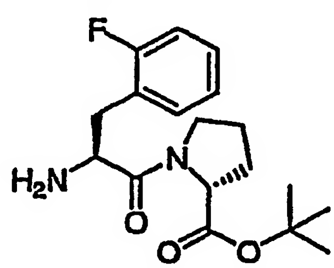
Compound (42)	Compound (43)
	
Compound (44)	**Compound (45)**
	
Compound (46)	**Compound (47)**
	
Compound (48)	**Compound (49)**
	

Table 2-6

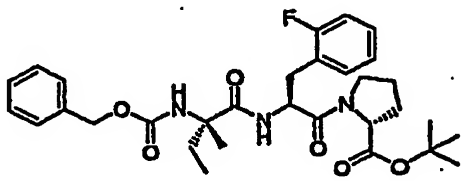
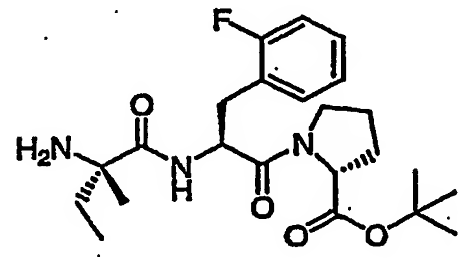
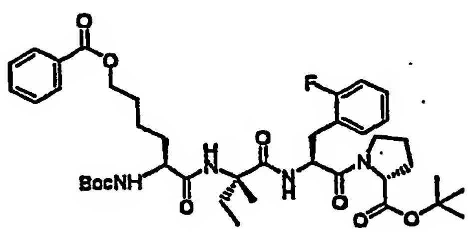
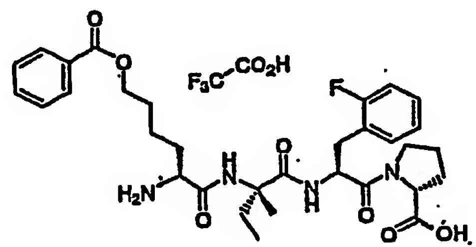
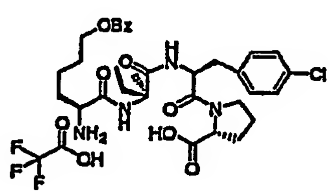
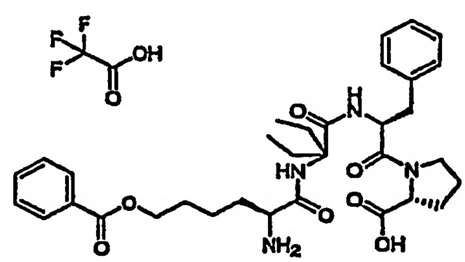
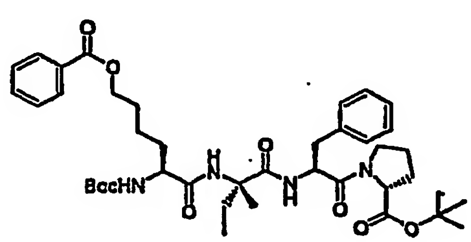
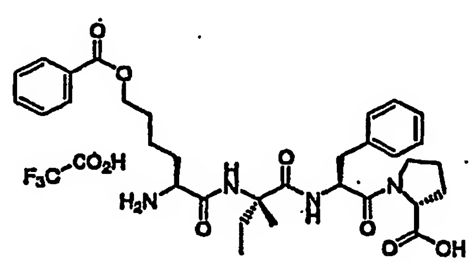
Compound (50)	Compound (51)
	
Compound (52)	Compound (53)
	
Compound (54)	Compound (55)
	
Compound (56)	Compound (57)
	

Table 2-7

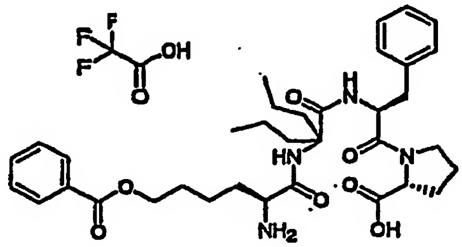
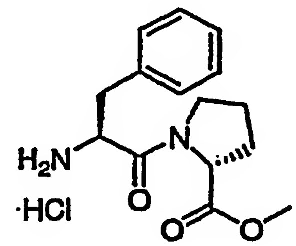
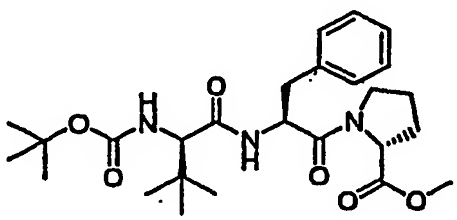
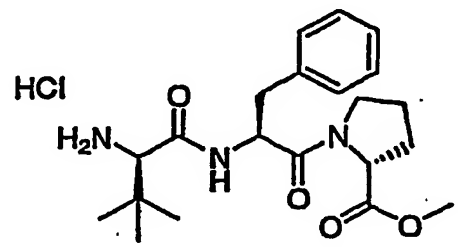
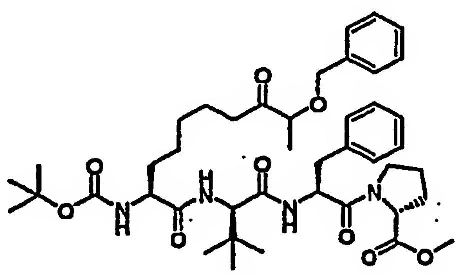
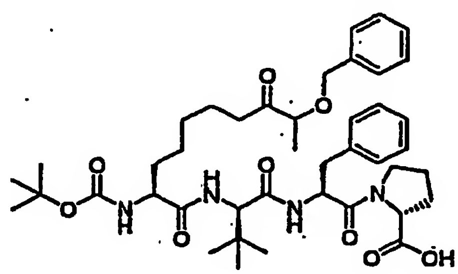
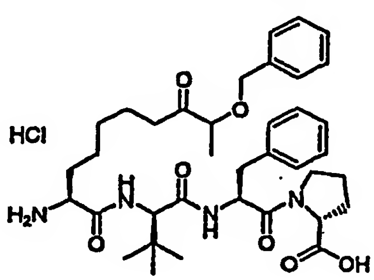
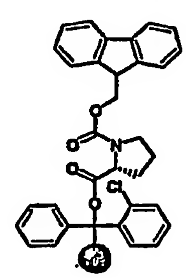
Compound (58)	Compound (59)
	
Compound (60)	Compound (61)
	
Compound (62)	Compound (63)
	
Compound (64)	Compound (65)
	

Table 2-8

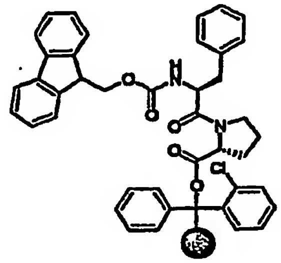
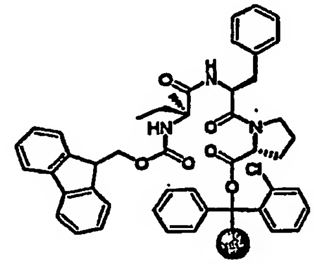
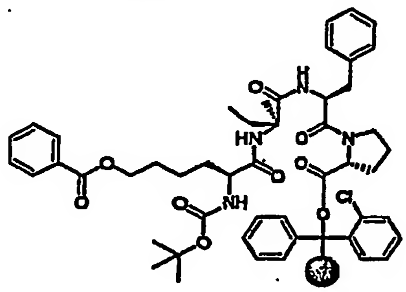
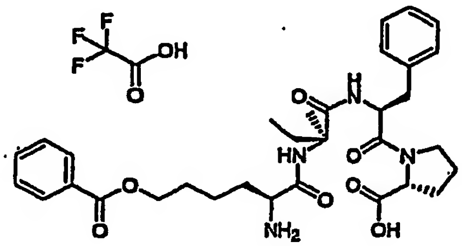
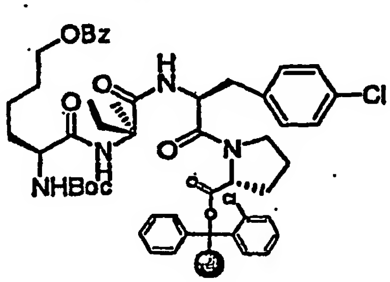
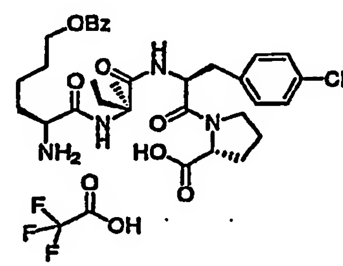
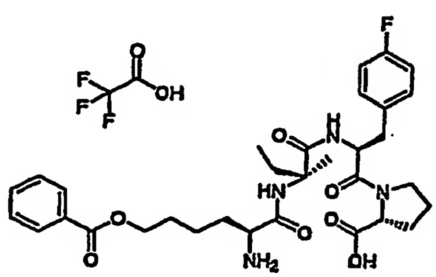
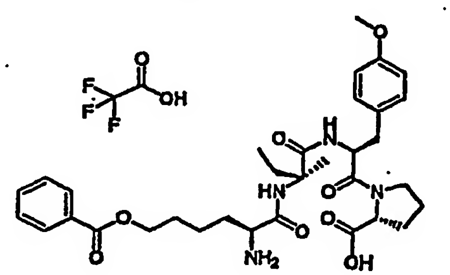
Compound (66)	Compound (67)
	
Compound (68)	**Compound (69)**
	
Compound (70)	**Compound (71)**
	
Compound (72)	**Compound (73)**
	

Table 2-9

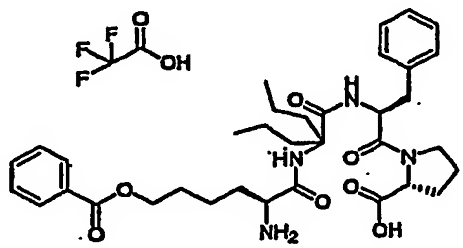
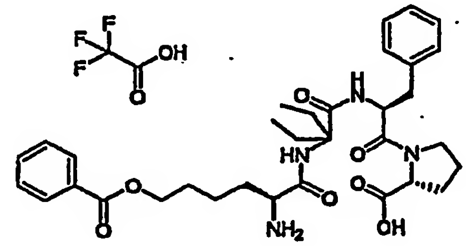
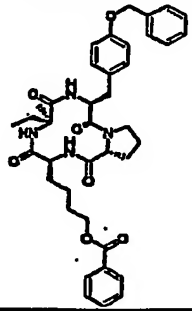
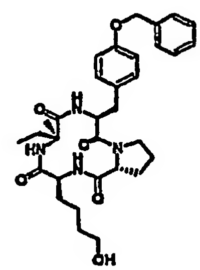
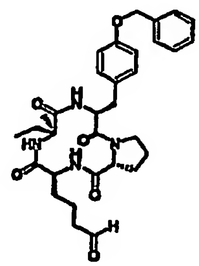
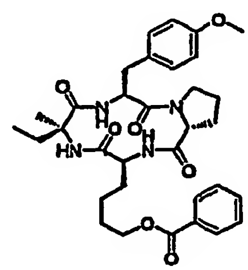
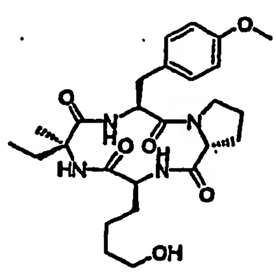
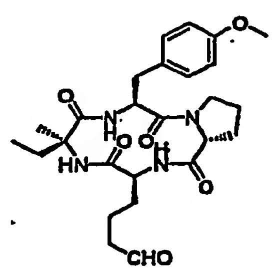
Compound (74)	Compound (75)
	
Compound (76)	Compound (77)
	
Compound (78)	Compound (79)
	
Compound (80)	Compound (81)
	

Table 2-10

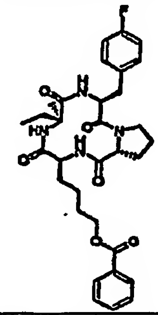
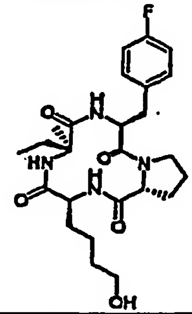
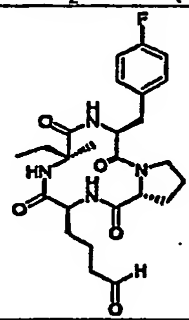
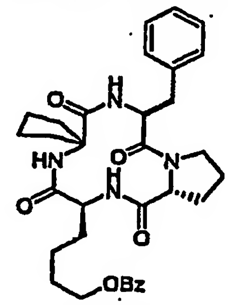
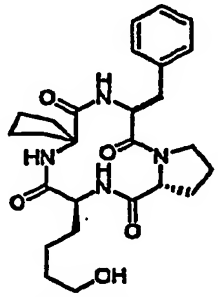
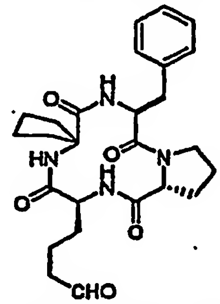
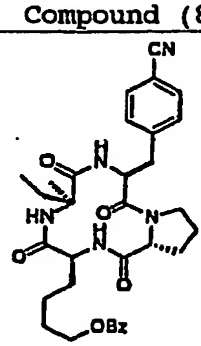
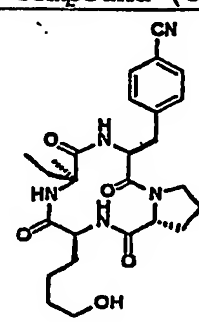
Compound (82)	Compound (83)
	
Compound (84)	Compound (85)
	
Compound (86)	Compound (87)
	
Compound (88)	Compound (89)
	

Table 2-11

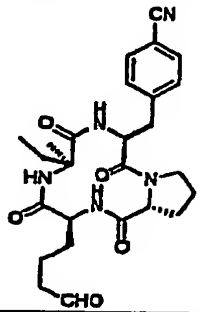
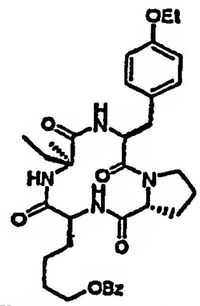
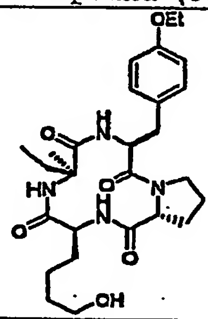
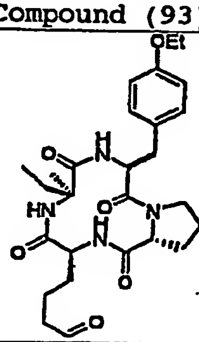
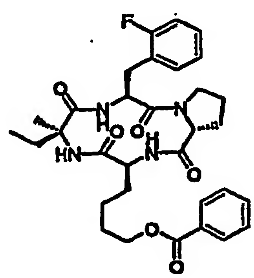
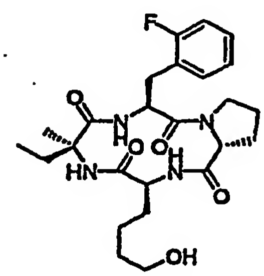
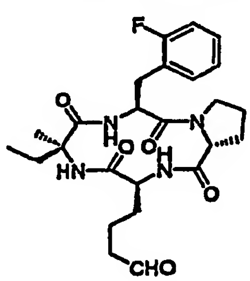
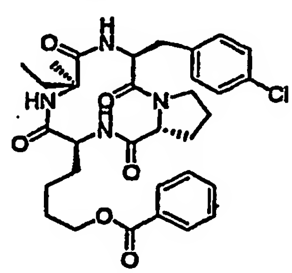
Compound (90)	Compound (91)
	
Compound (92)	Compound (93)
	
Compound (94)	Compound (95)
	
Compound (96)	Compound (97)
	

Table 2-12

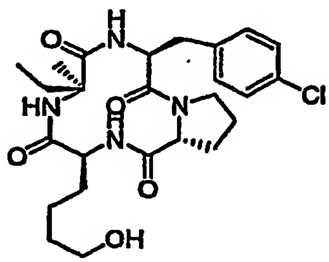
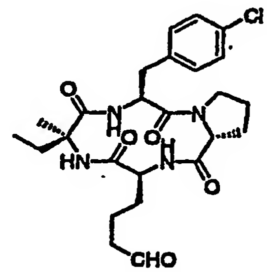
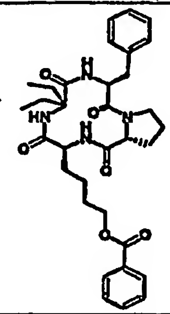
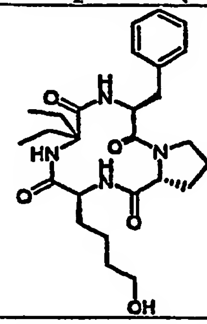
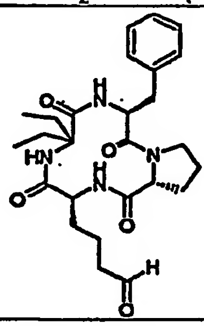
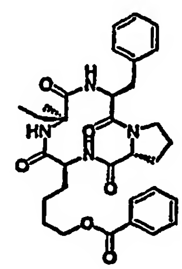
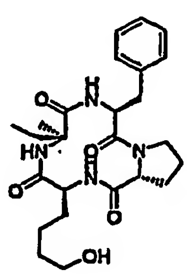
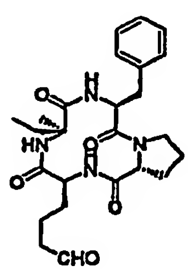
Compound (98)	Compound (99)
	
Compound (100)	Compound (101)
	
Compound (102)	Compound (103)
	
Compound (104)	Compound (105)
	

Table 2-13

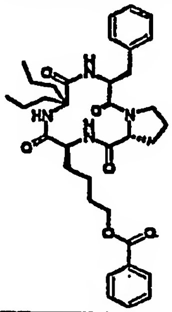
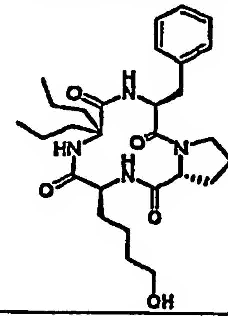
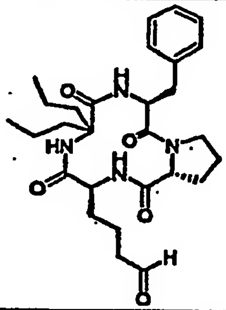
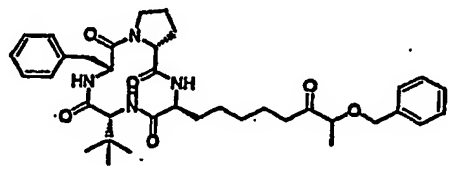
Compound (106)	Compound (107)
	
Compound (108)	**Compound (109)**
	

Table 2-14

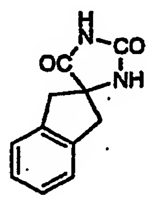
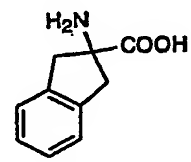
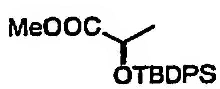
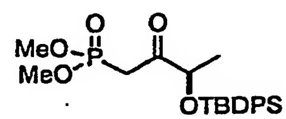
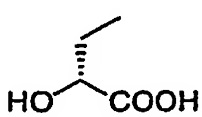
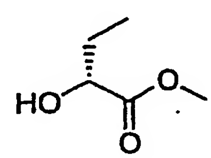
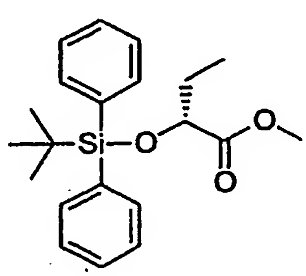
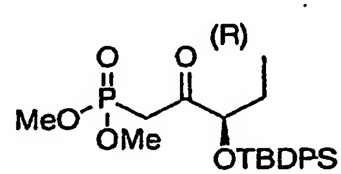
Compound (110)	Compound (111)
	
Compound (112)	**Compound (113)**
	
Compound (114)	**Compound (115)**
	
Compound (116)	**Compound (117)**
	

Table 2-15

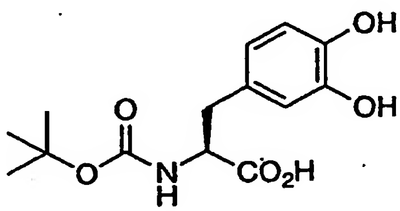
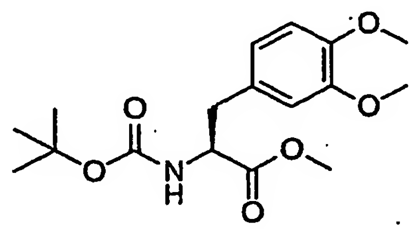
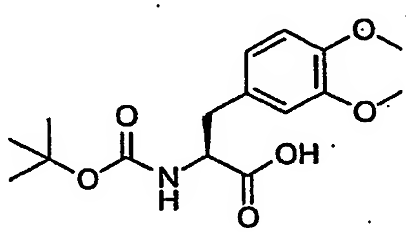
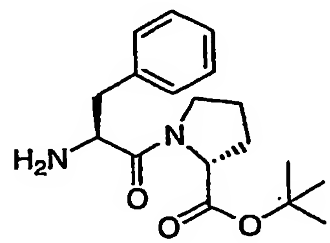
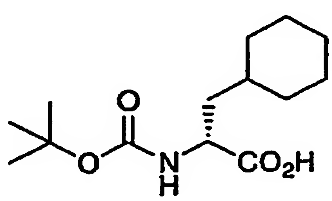
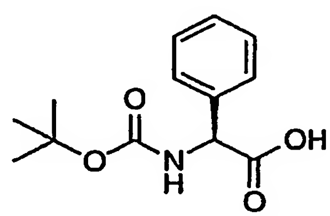
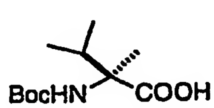
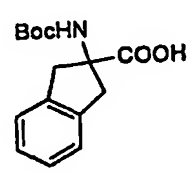
Compound (118)	Compound (119)
	
Compound (120)	Compound (121)
	
Compound (122)	Compound (123)
	
Compound (124)	Compound (125)
	

Table 2-16

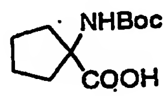
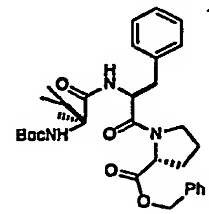
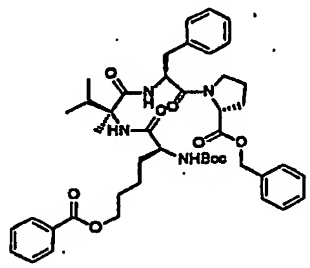
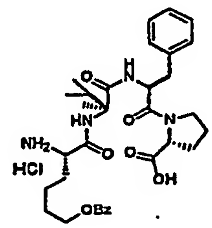
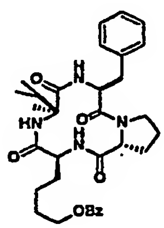
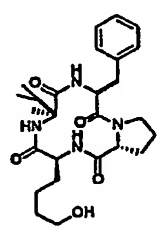
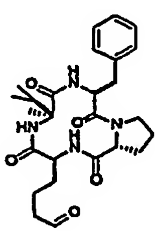
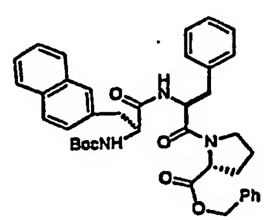
Compound (126)	Compound (127)
	
Compound (128)	**Compound (129)**
	
Compound (130)	**Compound (131)**
	
Compound (132)	**Compound (133)**
	

Table 2-17

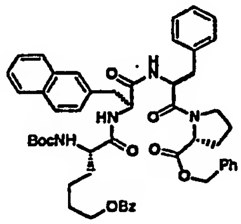
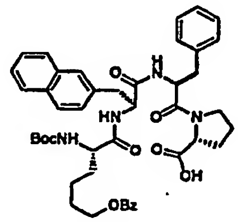
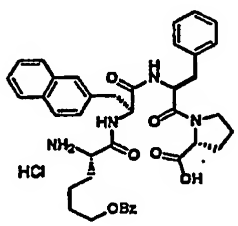
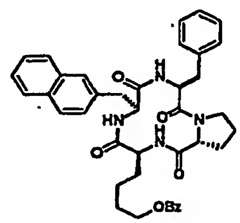
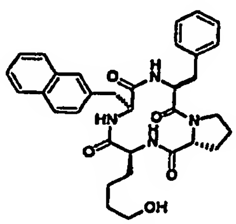
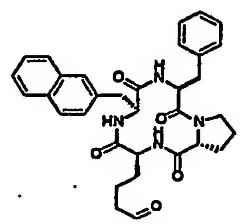
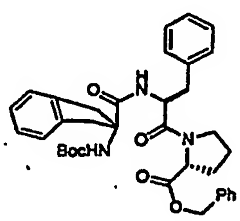
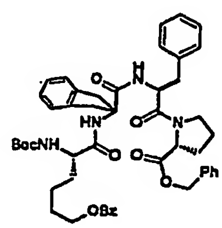
Compound (134)	Compound (135)
	
Compound (136)	**Compound (137)**
	
Compound (138)	**Compound (139)**
	
Compound (140)	**Compound (141)**
	

Table 2-18

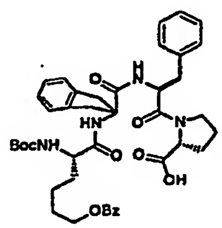
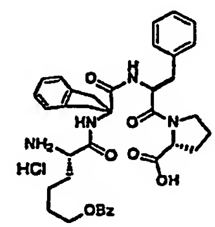
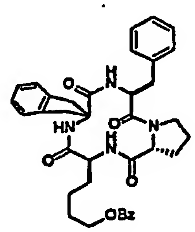
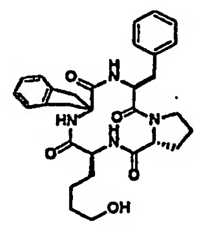
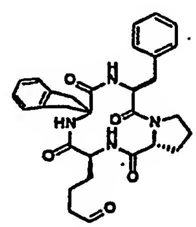
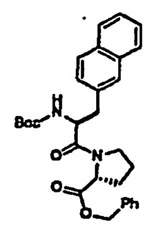
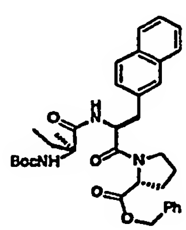
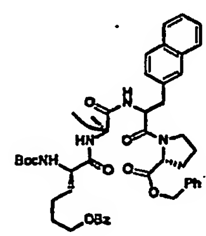
Compound (142)	Compound (143)
	
Compound (144)	**Compound (145)**
	
Compound (146)	**Compound (147)**
	
Compound (148)	**Compound (149)**
	

Table 2-19

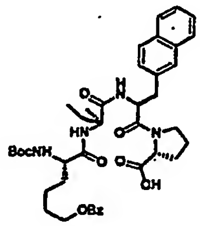
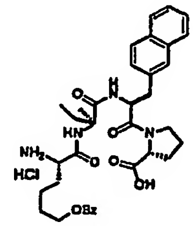
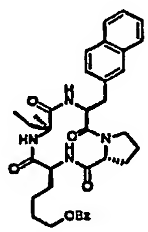
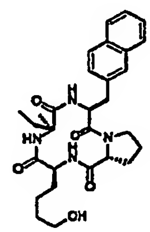
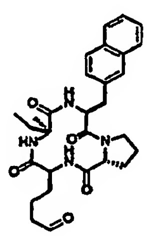
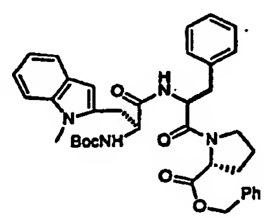
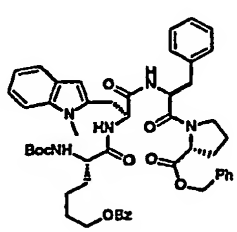
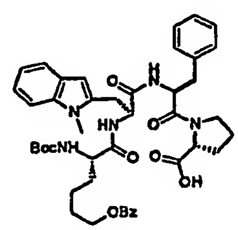
Compound (150)	Compound (151)
	
Compound (152)	Compound (153)
	
Compound (154)	Compound (155)
	
Compound (156)	Compound (157)
	

Table 2-20

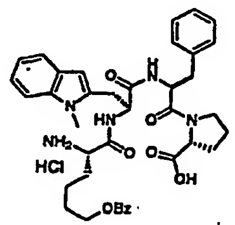
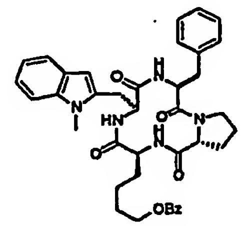
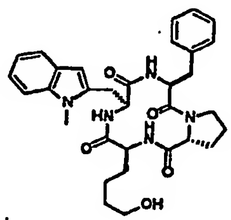
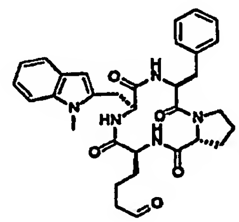
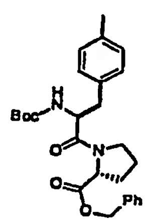
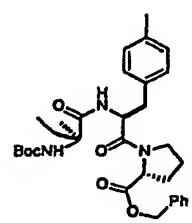
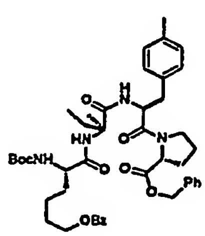
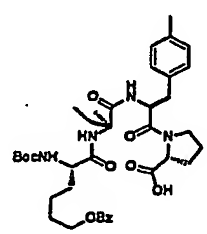
Compound (158)	Compound (159)
	
Compound (160)	Compound (161)
	
Compound (162)	Compound (163)
	
Compound (164)	Compound (165)
	

Table 2-21

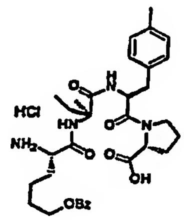
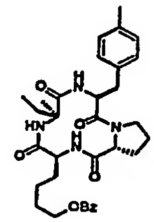
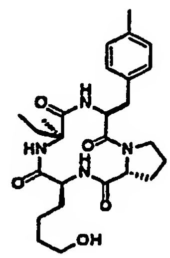
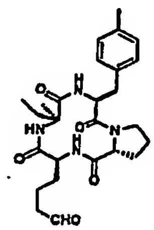
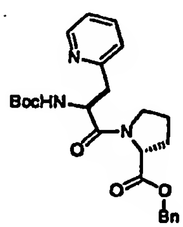
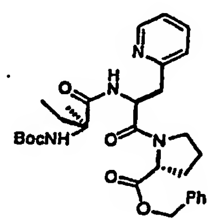
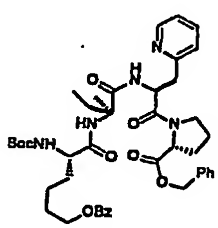
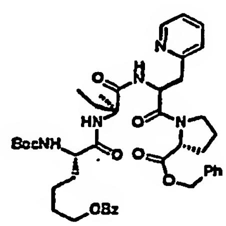
Compound (166)	Compound (167)
	
Compound (168)	**Compound (169)**
	
Compound (170)	**Compound (171)**
	
Compound (172)	**Compound (173)**
	

Table 2-22

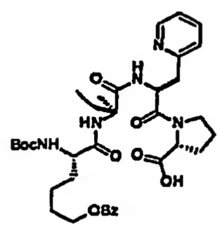
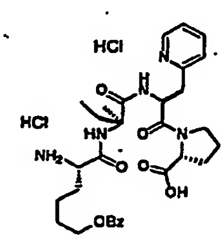
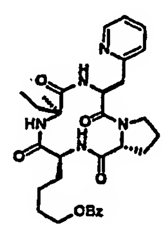
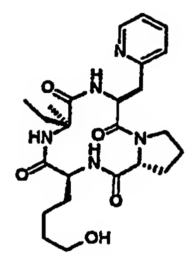
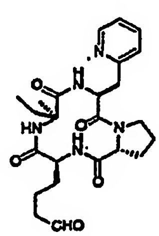
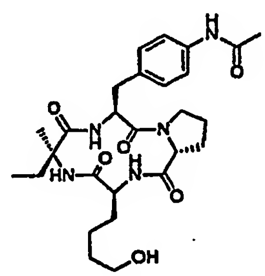
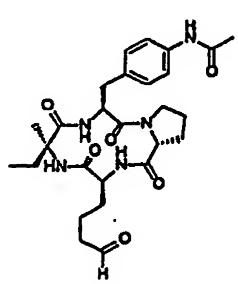
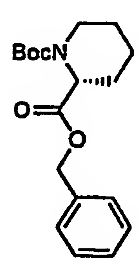
Compound (174)	Compound (175)
	
Compound (176)	Compound (177)
	
Compound (178)	Compound (179)
	
Compound (180)	Compound (181)
	

Table 2-23

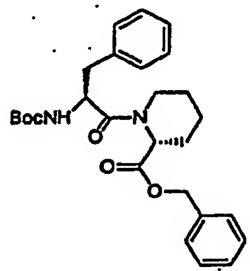
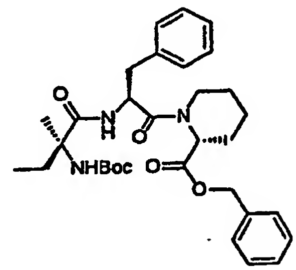
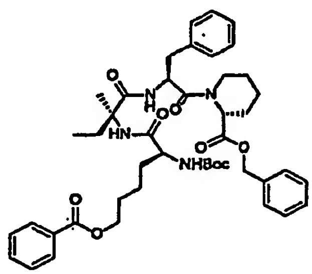
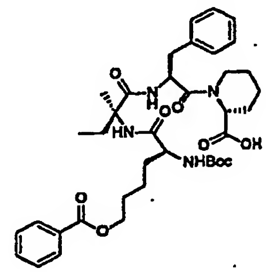
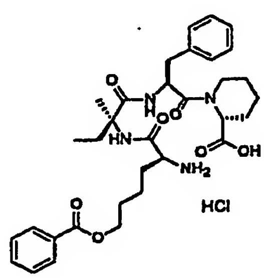
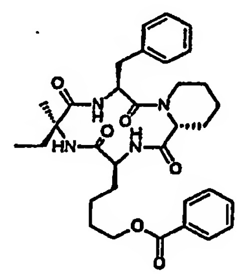
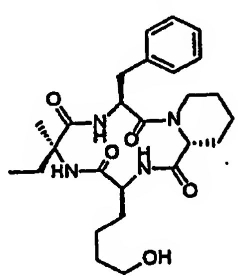
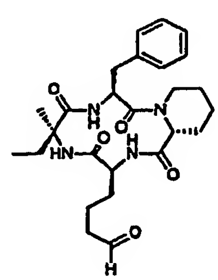
Compound (182)	Compound (183)
	
Compound (184)	**Compound (185)**
	
Compound (186)	**Compound (187)**
	
Compound (188)	**Compound (189)**
	

Table 2-24

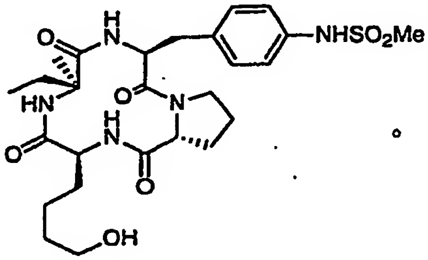
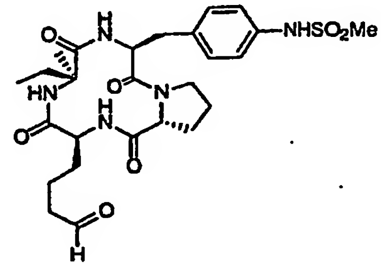
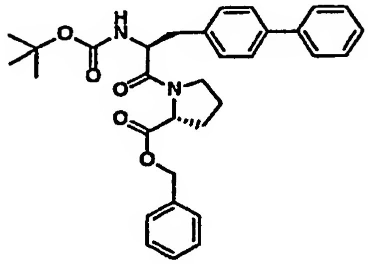
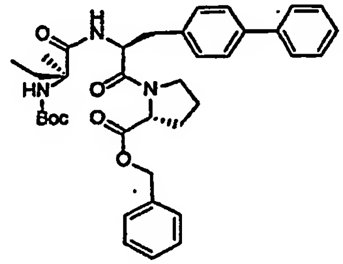
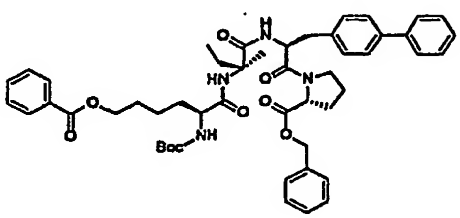
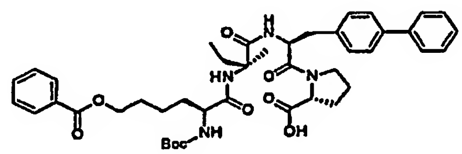
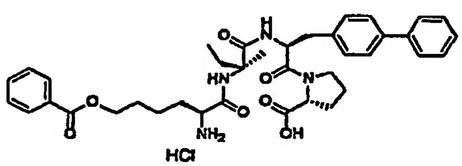
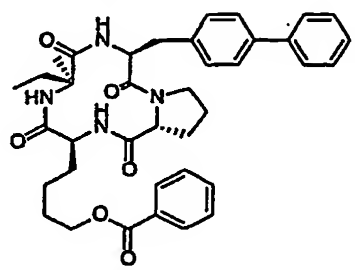
Compound (190)	Compound (191)
	
Compound (192)	Compound (193)
	
Compound (194)	Compound (195)
	
Compound (196)	Compound (197)
	

Table 2-25

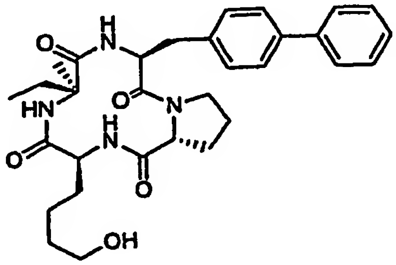
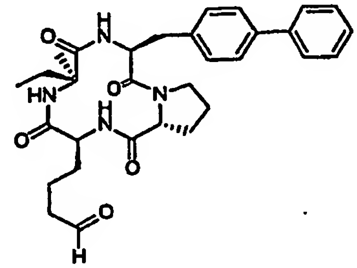
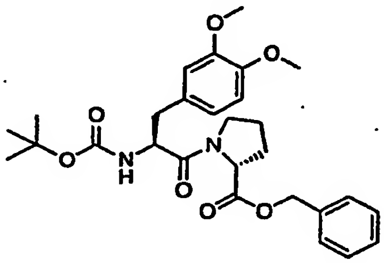
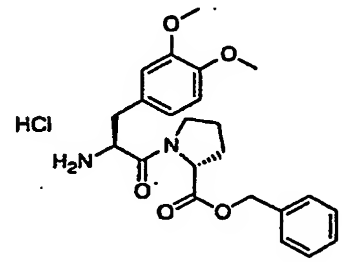
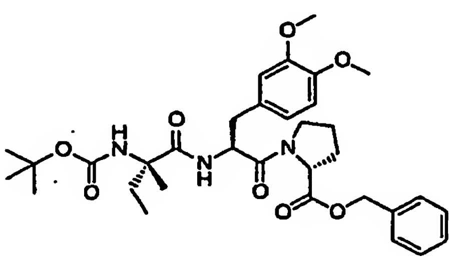
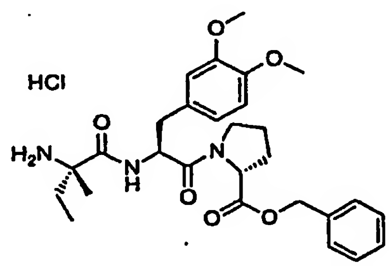
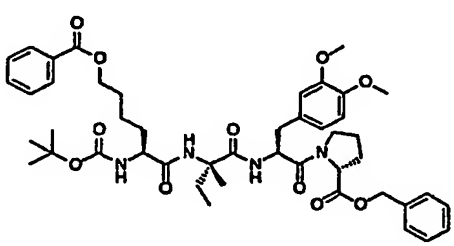
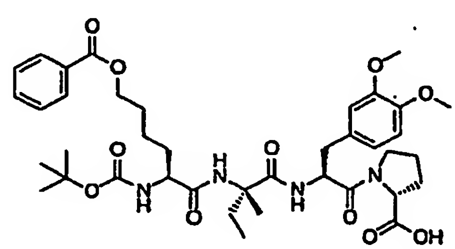
Compound (198)	Compound (199)
	
Compound (200)	**Compound (201)**
	
Compound (202)	**Compound (203)**
	
Compound (204)	**Compound (205)**
	

Table 2-26

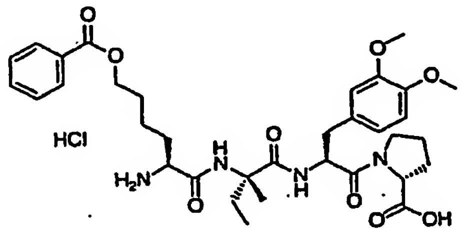
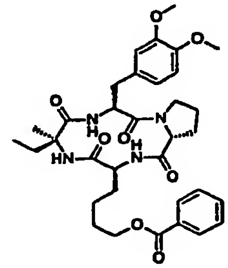
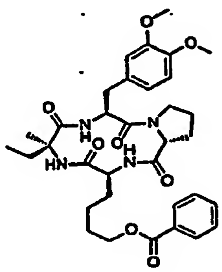
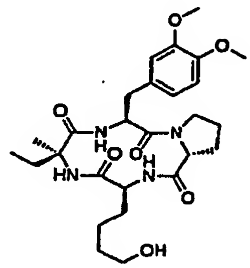
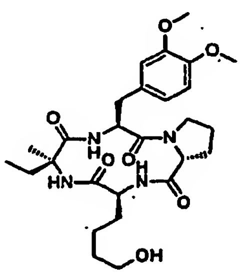
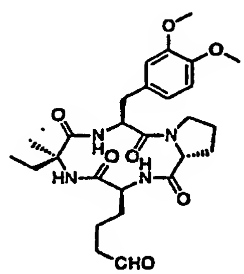
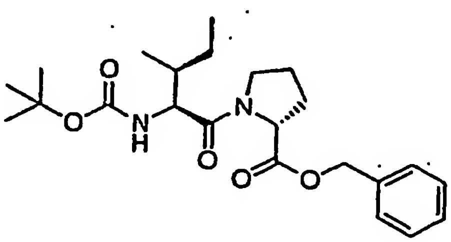
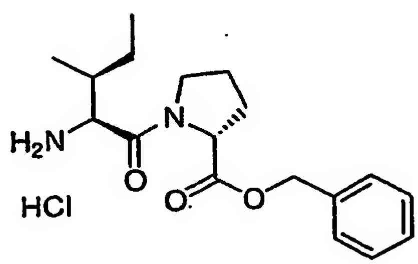
Compound (206)	Compound (207)
	
Compound (208)	**Compound (209)**
	
Compound (210)	**Compound (211)**
	
Compound (212)	**Compound (213)**
	

Table 2-27

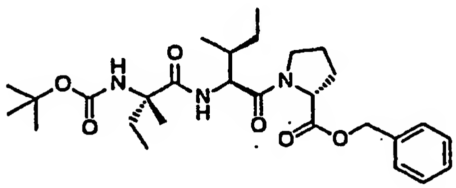
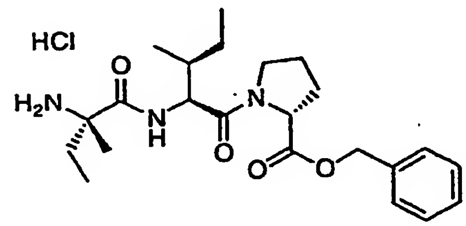
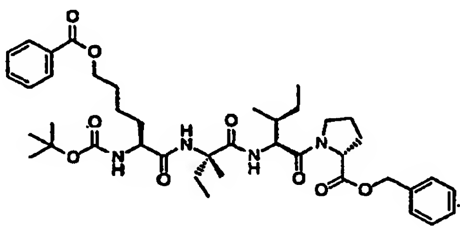
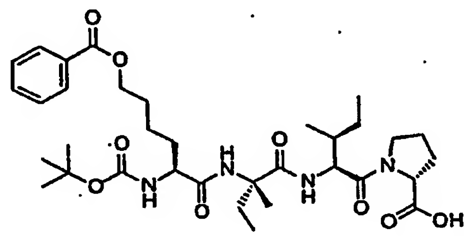
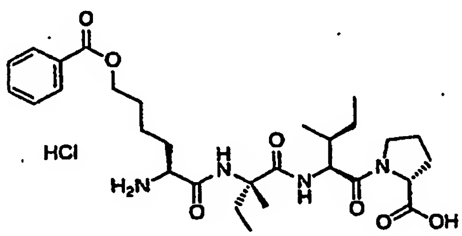
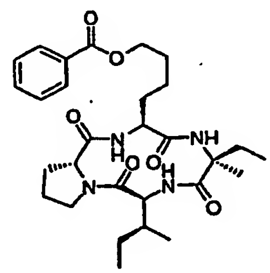
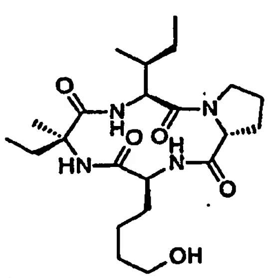
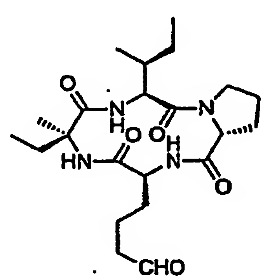
Compound (214)	Compound (215)
	
Compound (216)	**Compound (217)**
	
Compound (218)	**Compound (219)**
	
Compound (220)	**Compound (221)**
	

Table 2-28

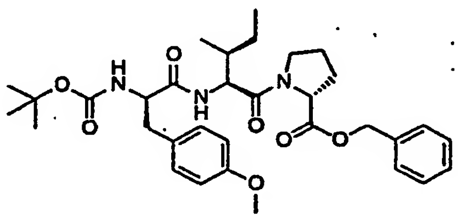
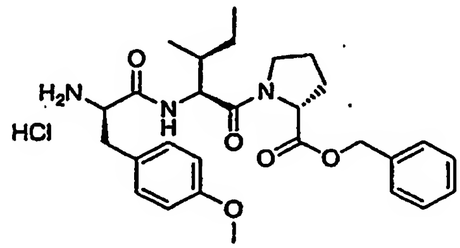
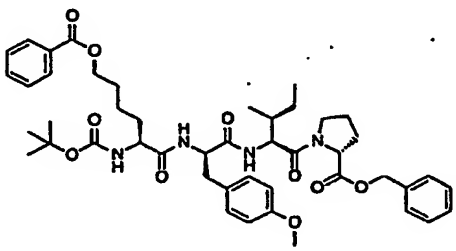
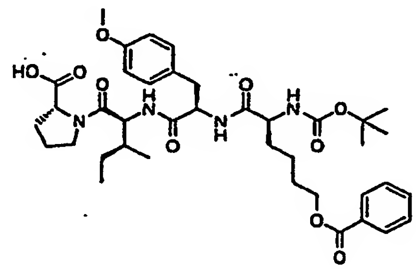
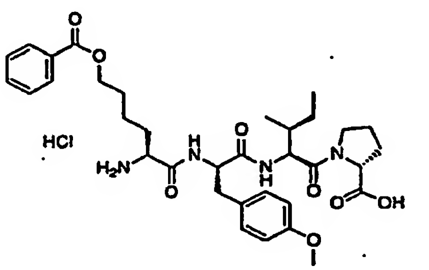
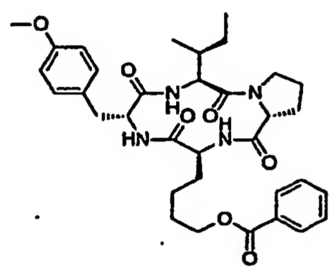
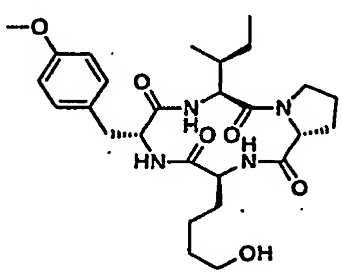
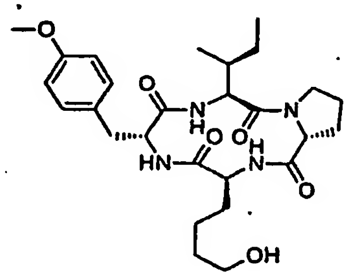
Compound (222)	Compound (223)
	
Compound (224)	**Compound (225)**
	
Compound (226)	**Compound (227)**
	
Compound (228)	**Compound (229)**
	

Table 2-29

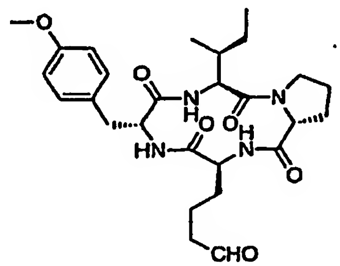
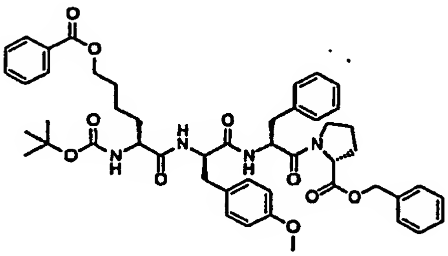
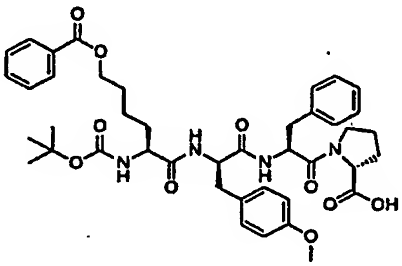
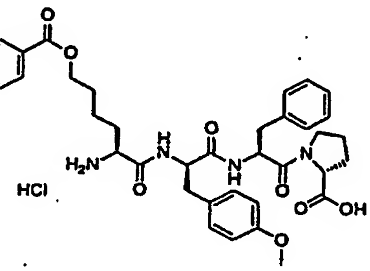
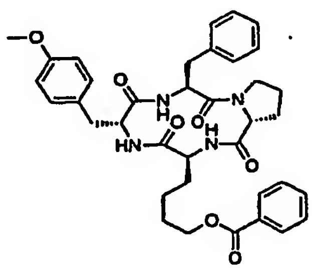
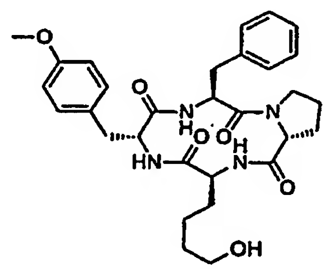
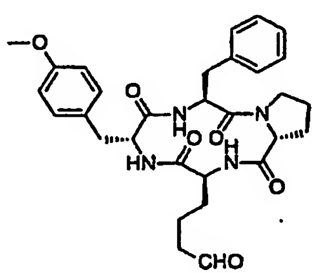
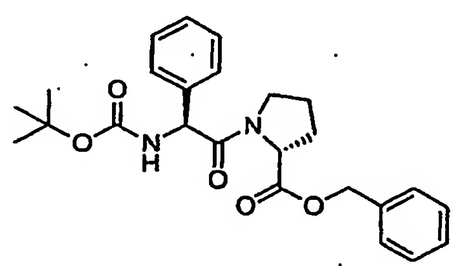
Compound (230)	Compound (231)
	
Compound (232)	**Compound (233)**
	
Compound (234)	**Compound (235)**
	
Compound (236)	**Compound (237)**
	

Table 2-30

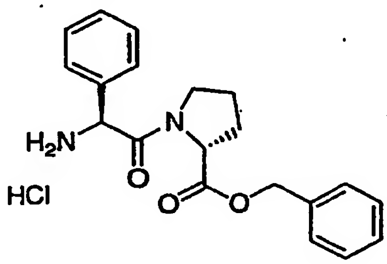
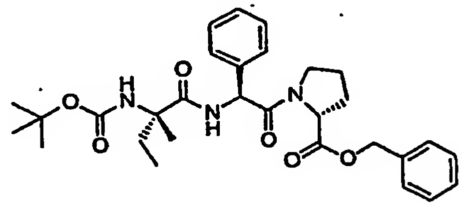
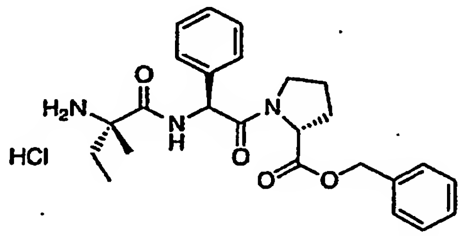
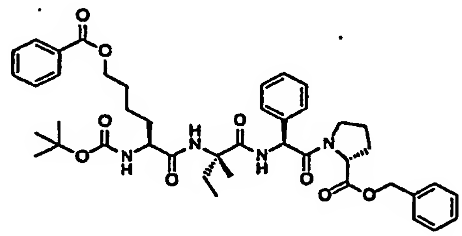
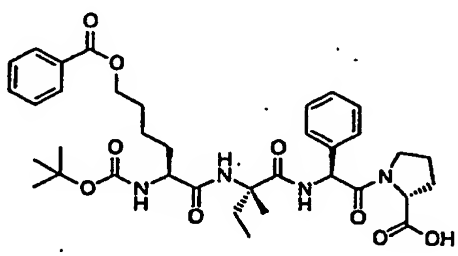
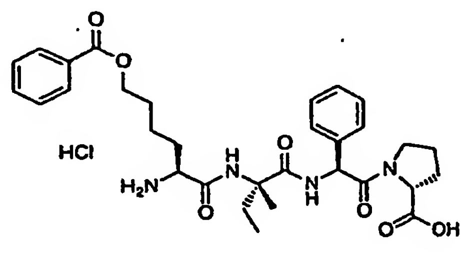
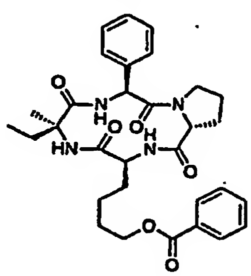
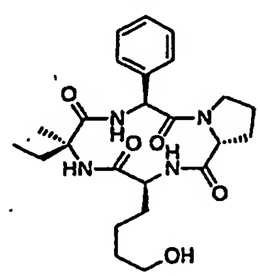
Compound (238)	Compound (239)
	
Compound (240)	**Compound (241)**
	
Compound (242)	**Compound (243)**
	
Compound (244)	**Compound (245)**
	

Table 2-31

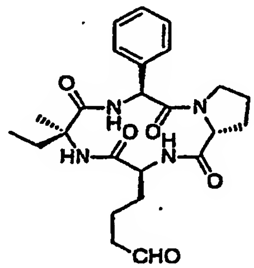
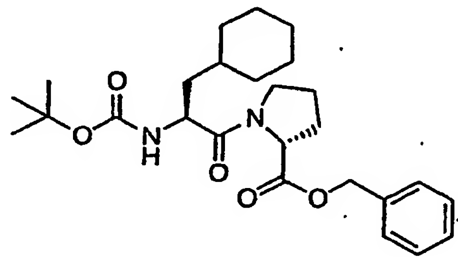
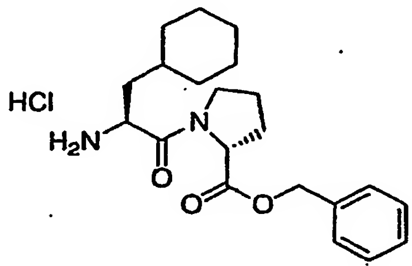
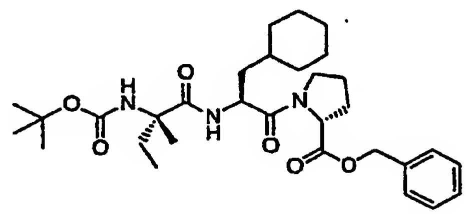
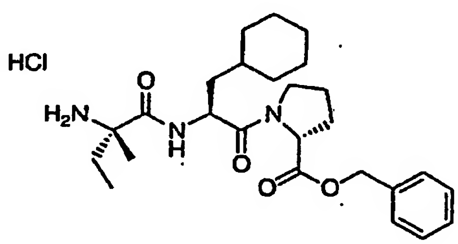
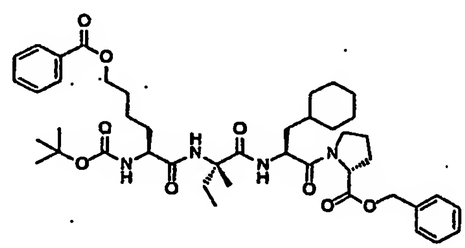
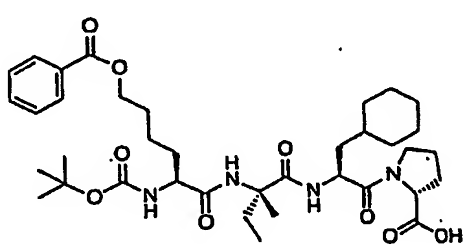
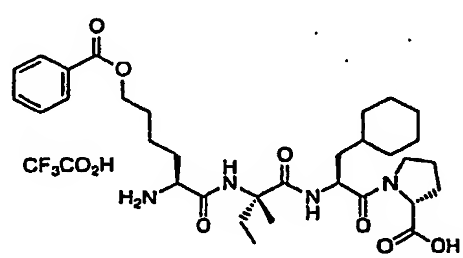
Compound (246)	Compound (247)
	
Compound (248)	**Compound (249)**
	
Compound (250)	**Compound (251)**
	
Compound (252)	**Compound (253)**
	

Table 2-32

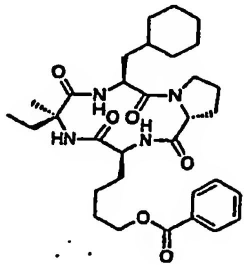
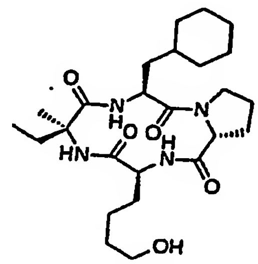
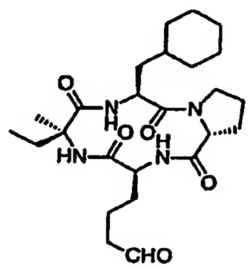
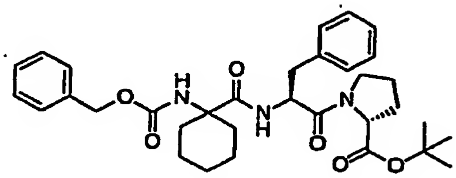
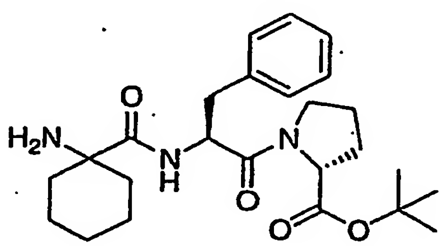
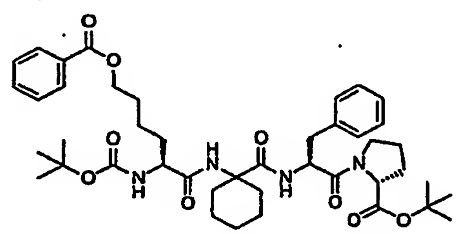
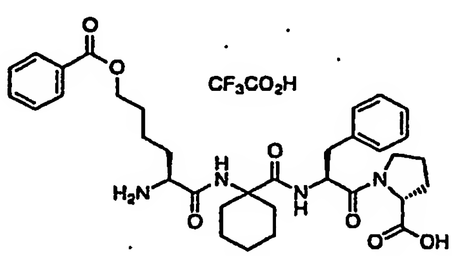
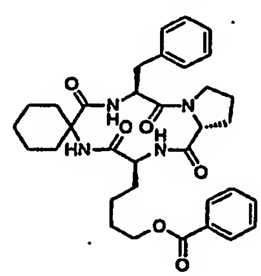
Compound (254)	Compound (255)
	
Compound (256)	Compound (257)
	
Compound (258)	Compound (259)
	
Compound (260)	Compound (261)
	

Table 2-33

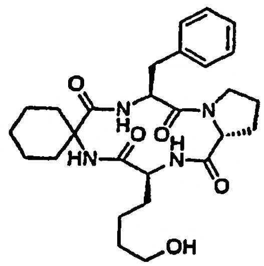
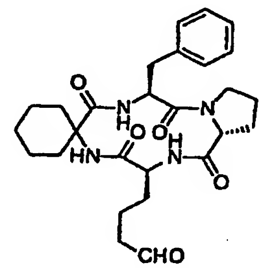
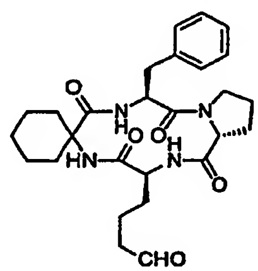
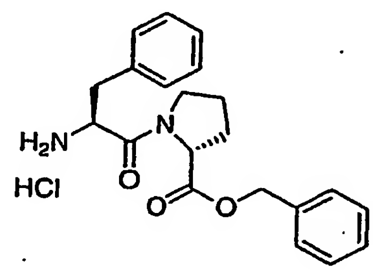
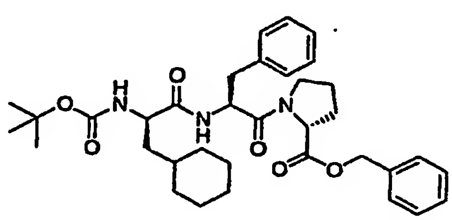
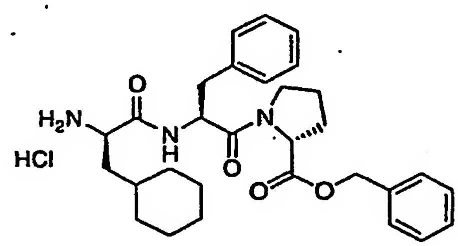
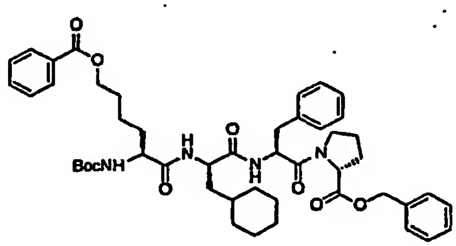
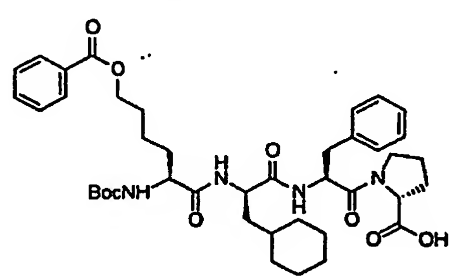
Compound (262)	Compound (263)
	
Compound (264)	Compound (265)
	
Compound (266)	Compound (267)
	
Compound (268)	Compound (269)
	

Table 2-34

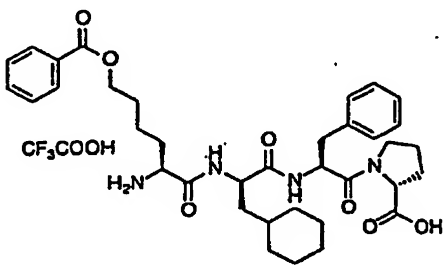
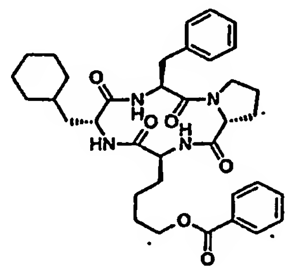
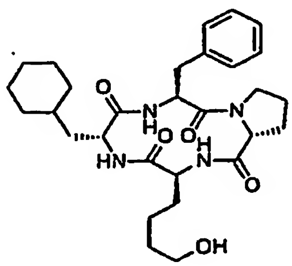
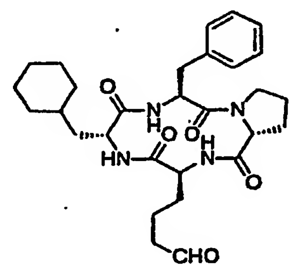
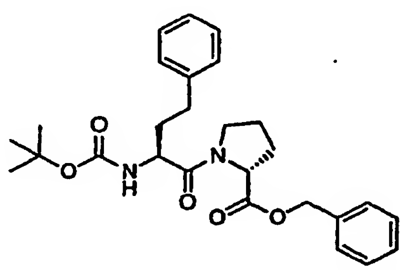
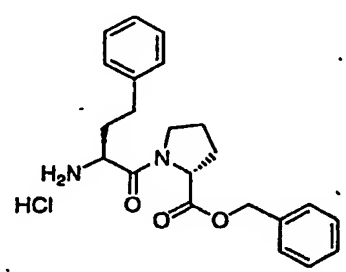
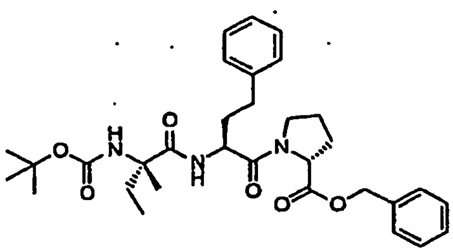
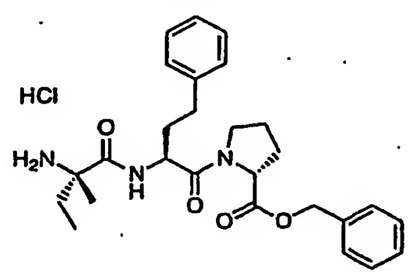
Compound (270)	Compound (271)
	
Compound (272)	**Compound (273)**
	
Compound (274)	**Compound (275)**
	
Compound (276)	**Compound (277)**
	

Table 2-35

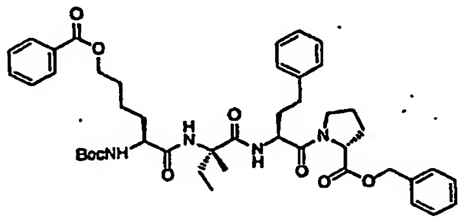
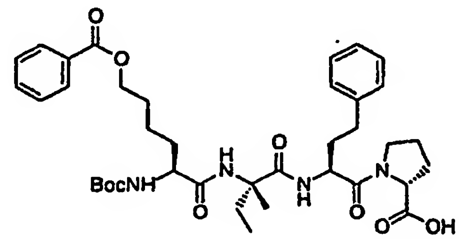
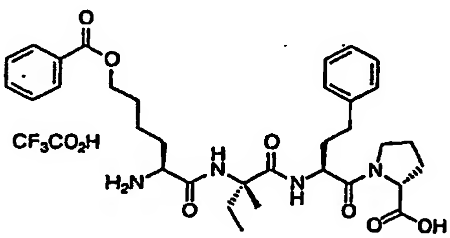
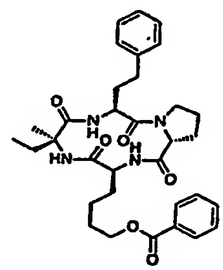
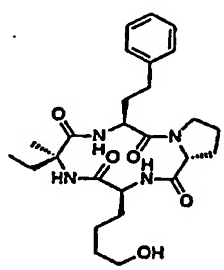
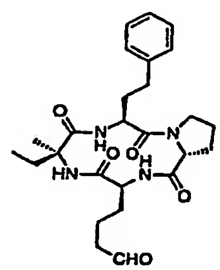
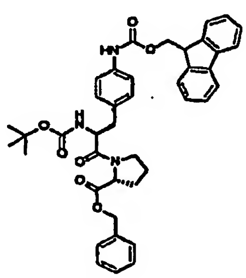
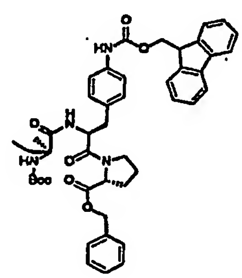
Compound (278)	Compound (279)
	
Compound (280)	**Compound (281)**
	
Compound (282)	**Compound (283)**
	
Compound (284)	**Compound (285)**
	

Table 2-36

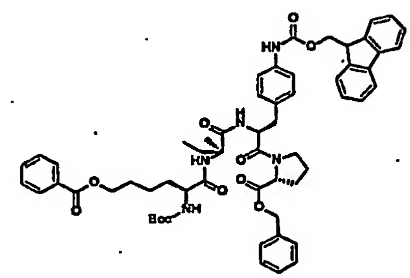
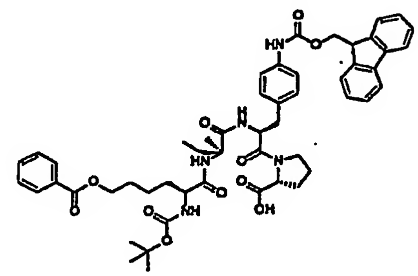
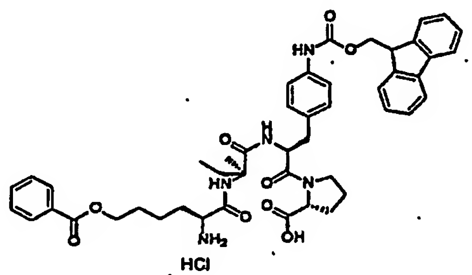
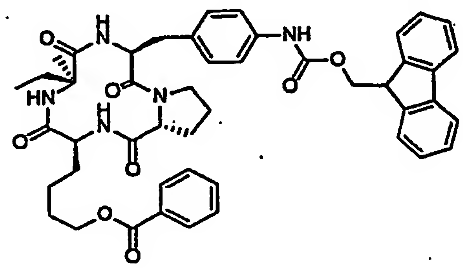
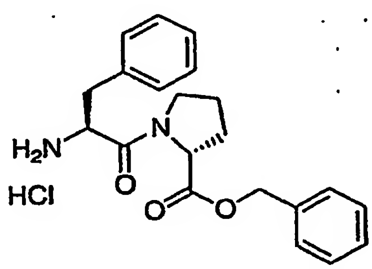
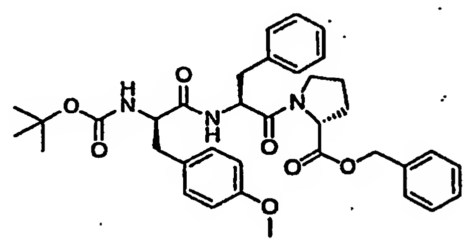
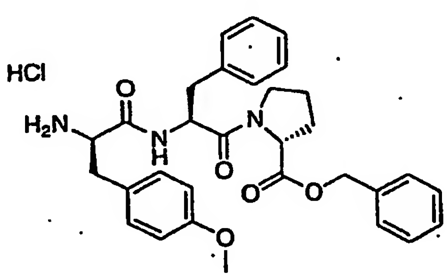
Compound (286)	Compound (287)
	
Compound (288)	**Compound (289)**
	
Compound (290)	**Compound (291)**
	
Compound (292)	
	

Table 2-37

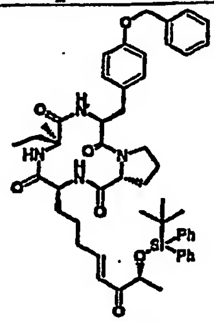
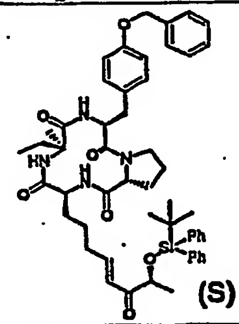
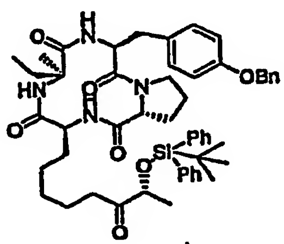
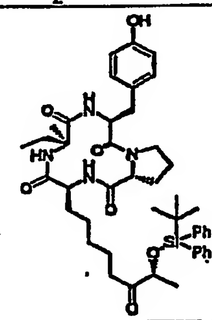
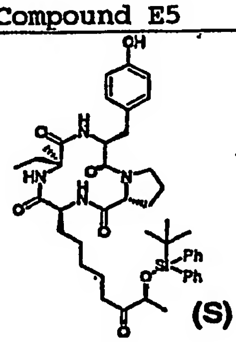
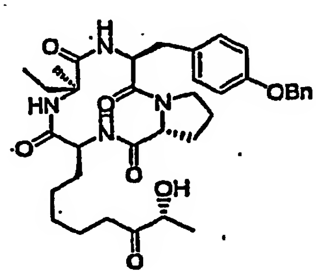
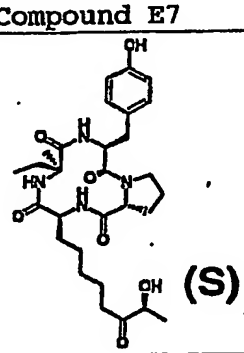
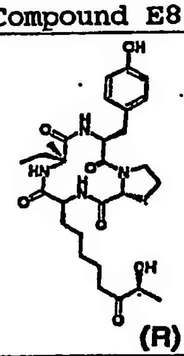
Compound E1	Compound E2
	
Compound E3	Compound E4
	
Compound E5	Compound E6
	
Compound E7	Compound E8
	

Table 2-38

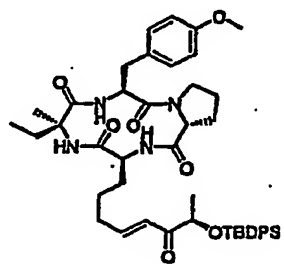
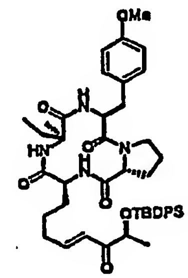
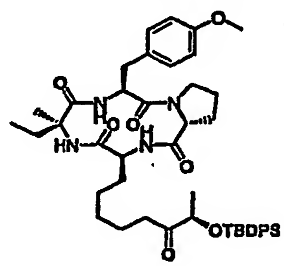
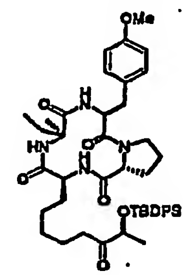
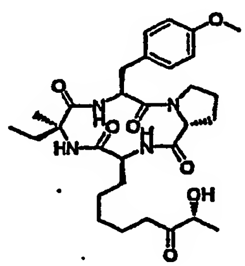
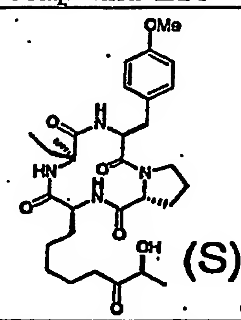
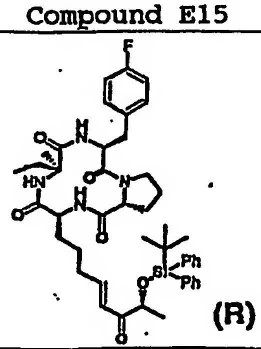
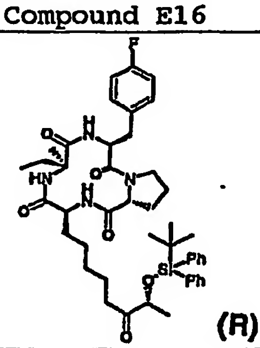
Compound E9	Compound E10
	
Compound E11	Compound E12
	
Compound E13	Compound E14
	
Compound E15	Compound E16
	

Table 2-39

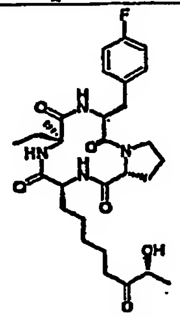
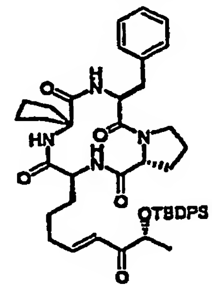
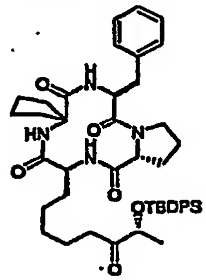
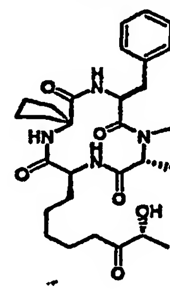
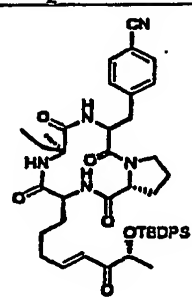
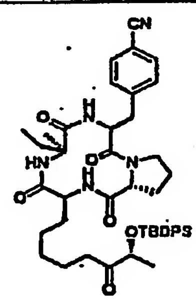
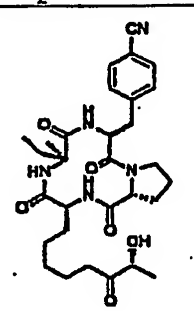
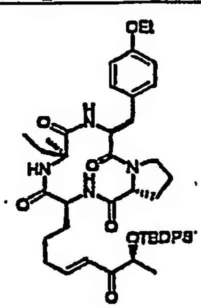
Compound E17	Compound E18
 (R)	
Compound E19	**Compound E20**
	 (R)
Compound E21	**Compound E22**
	
Compound E23	**Compound E24**
	

Table 2-40

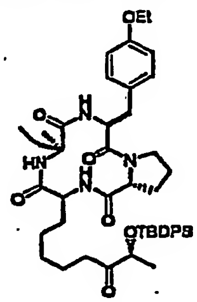
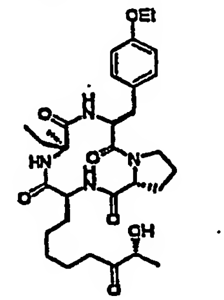
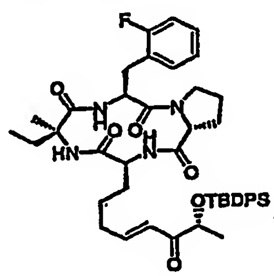
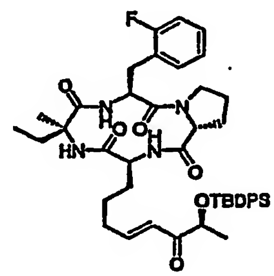
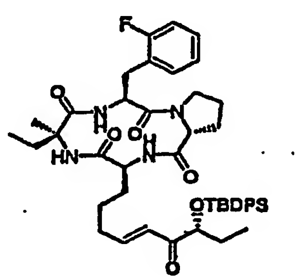
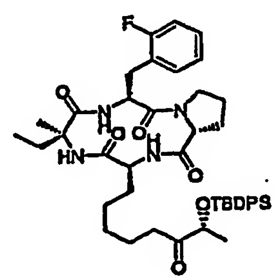
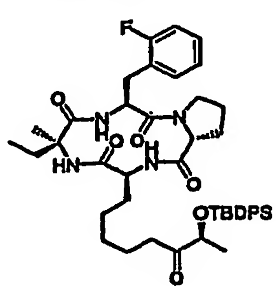
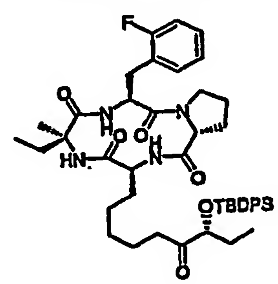
Compound E25	Compound E26
	
Compound E27	Compound E28
	
Compound E29	Compound E30
	
Compound E31	Compound E32
	

Table 2-41

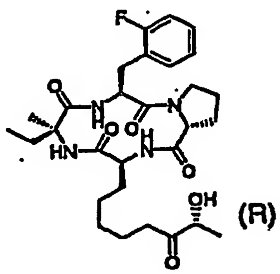
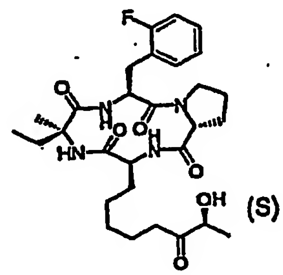
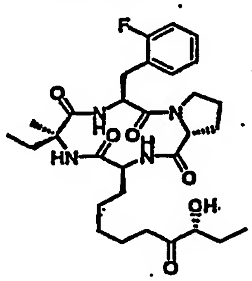
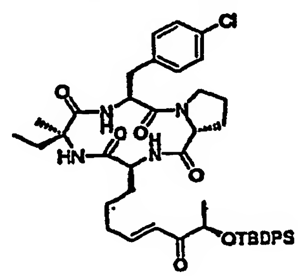
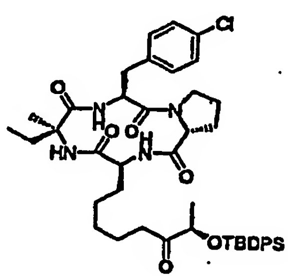
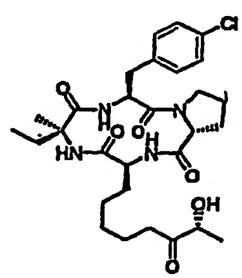
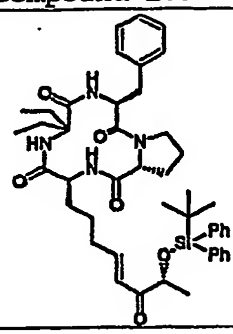
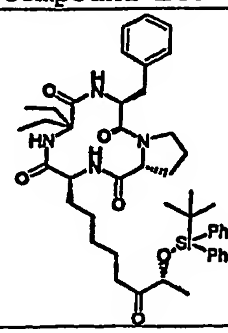
Compound E33	Compound E34
	
Compound E35	**Compound E36**
	
Compound E37	**Compound E38**
	
Compound E39	**Compound E40**
	

Table 2-42

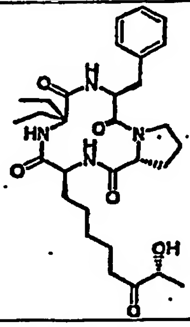
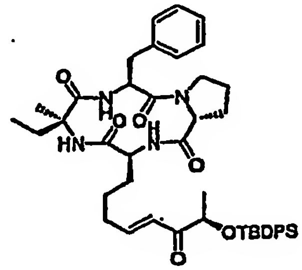
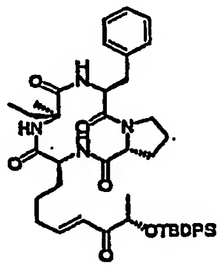
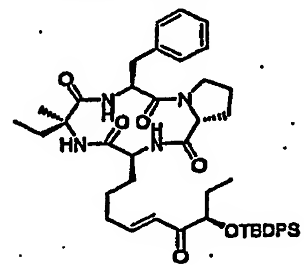
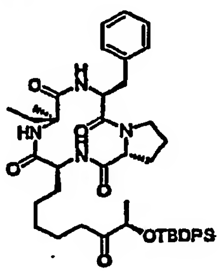
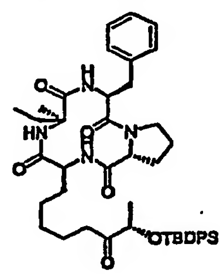
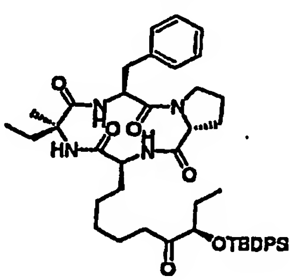
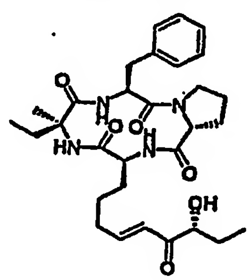
Compound E41	Compound E42
	
Compound E43	**Compound E44**
	
Compound E45	**Compound E46**
	
Compound E47	**Compound E48**
	

Table 2-43

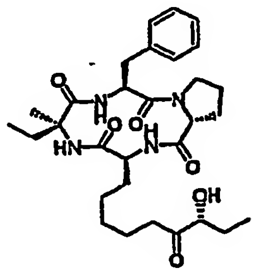
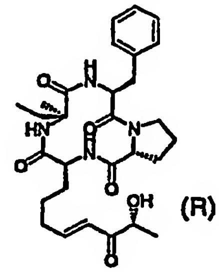
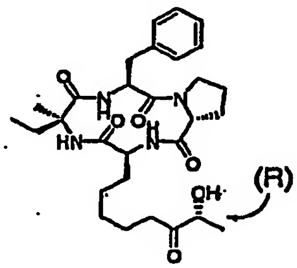
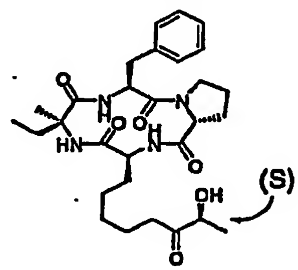
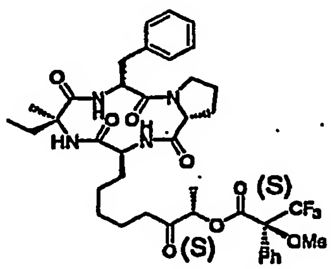
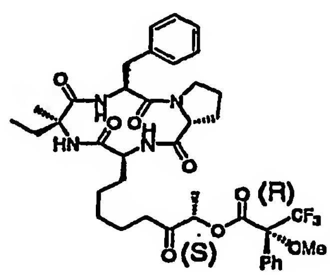
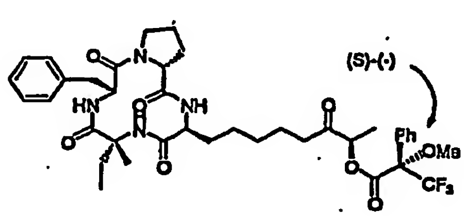
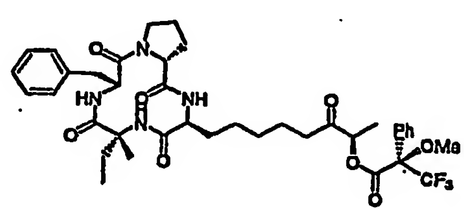
Compound E49	Compound E50
	
Compound E51	**Compound E52**
	
Compound E53	**Compound E54**
	
Compound E55	**Compound E56**
	

Table 2-44

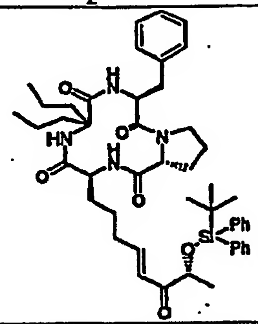
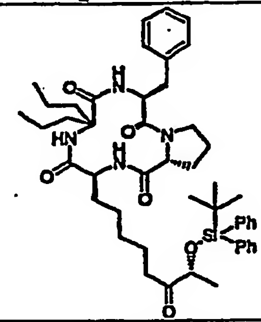
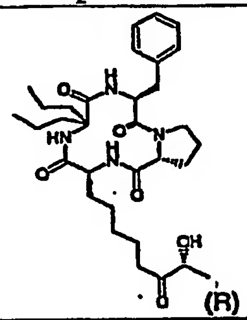
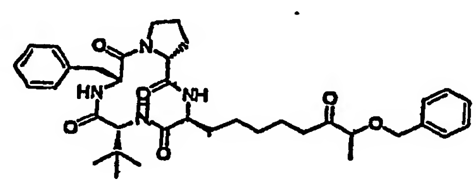
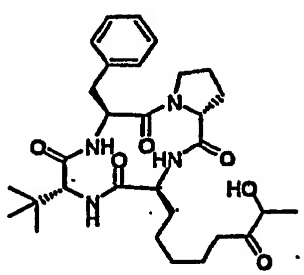
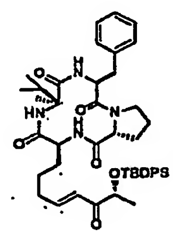
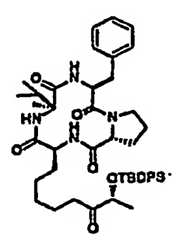
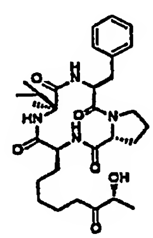
Compound E57	Compound E58
	
Compound E59	**Compound E60**
	
Compound E61	**Compound E62**
	
Compound E63	**Compound E64**
	

Table 2-45

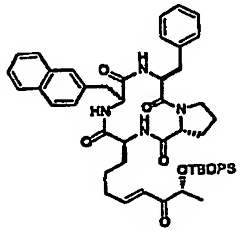
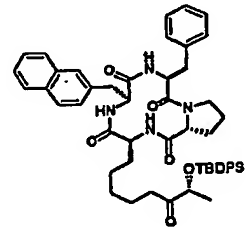
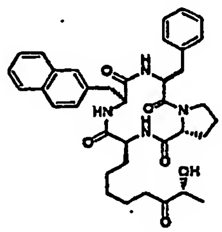
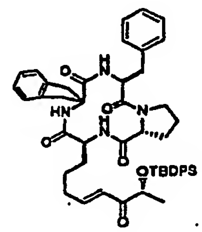
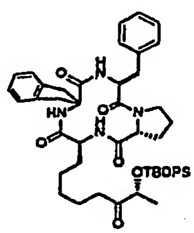
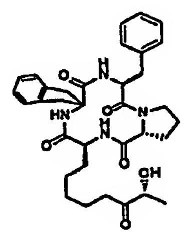
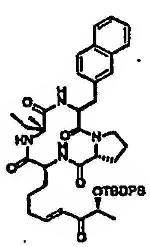
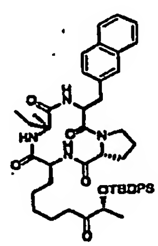
Compound E65	Compound E66
	
Compound E67	**Compound E68**
	
Compound E69	**Compound E70**
	
Compound E71	**Compound E72**
	

Table 2-46

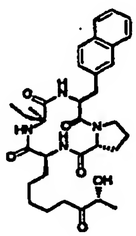
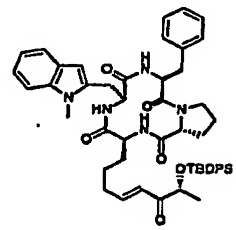
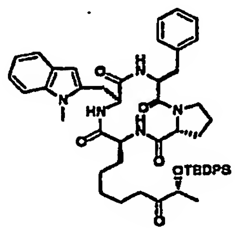
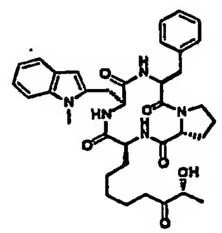
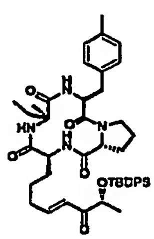
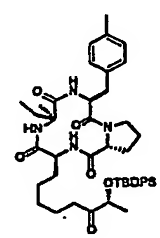
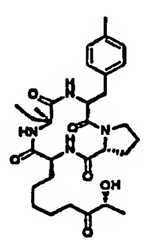
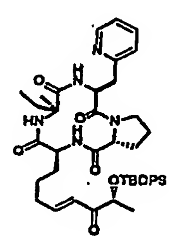
Compound E73	Compound E74
	
Compound E75	**Compound E76**
	
Compound E77	**Compound E78**
	
Compound E79	**Compound E80**
	

Table 2-47

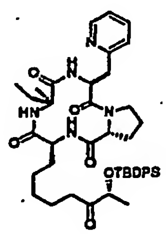
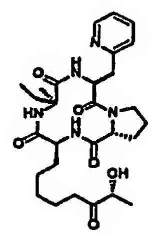
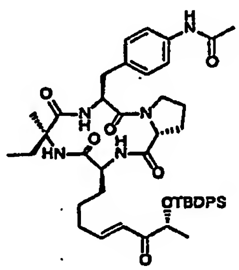
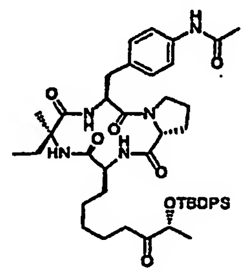
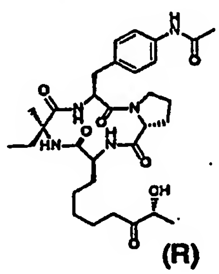
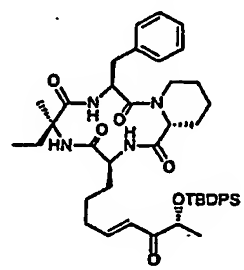
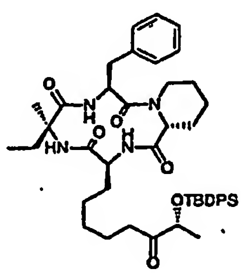
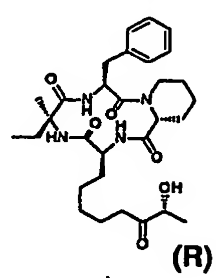
Compound E81	Compound E82
	
Compound E83	**Compound E84**
	
Compound E85	**Compound E86**
	
Compound E87	**Compound E88**
	

Table 2-48

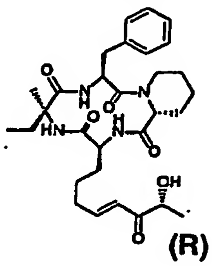
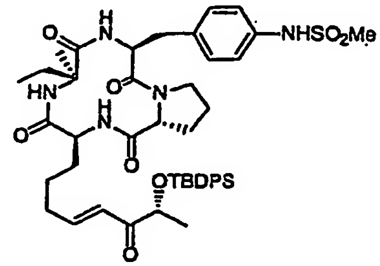
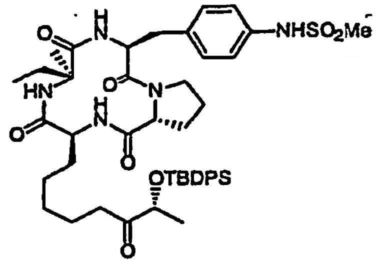
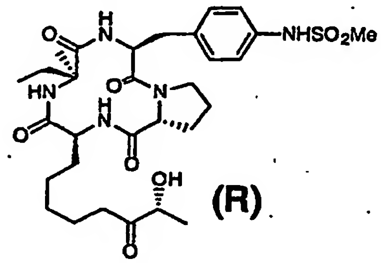
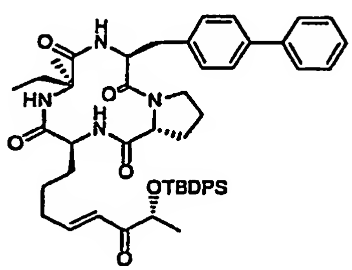
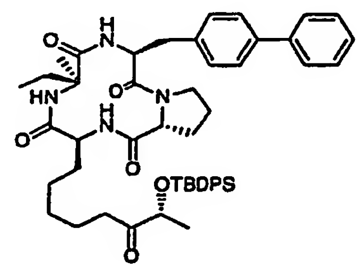
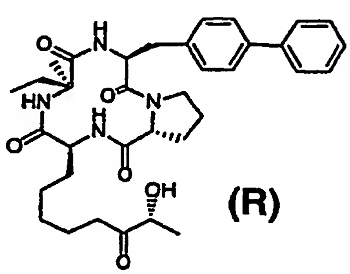
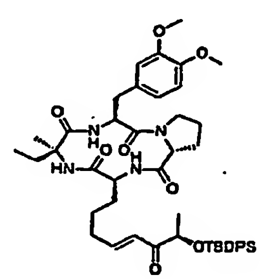
Compound E89	Compound E90
	
Compound E91	**Compound E92**
	
Compound E93	**Compound E94**
	
Compound E95	**Compound E96**
	

Table 2-49

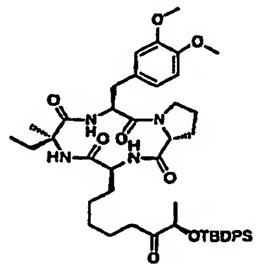
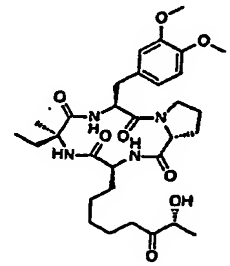
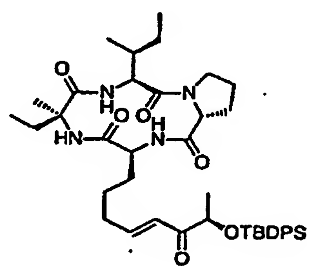
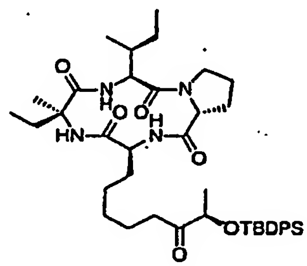
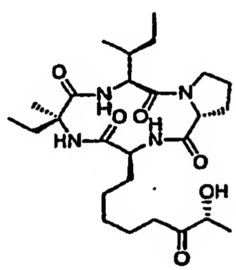
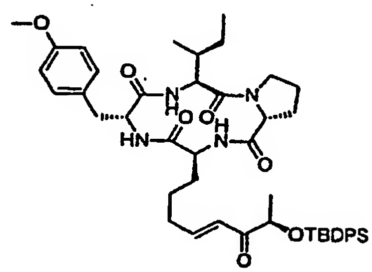
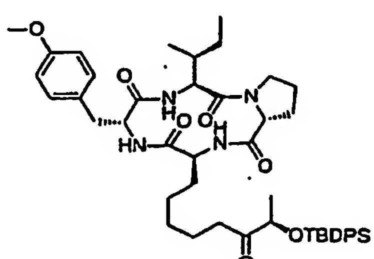
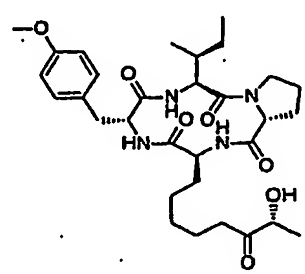
Compound E97	Compound E98
	
Compound E99	**Compound E100**
	
Compound E101	**Compound E102**
	
Compound E103	**Compound E104**
	

Table 2-50

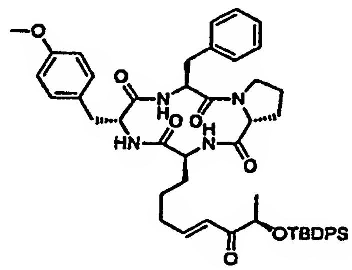
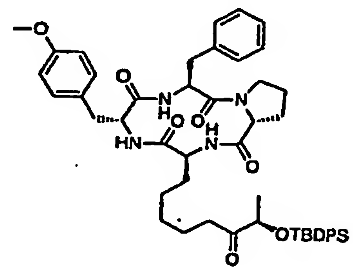
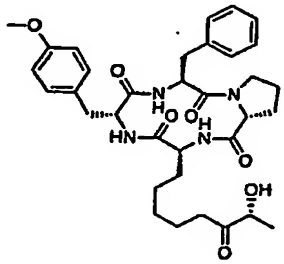
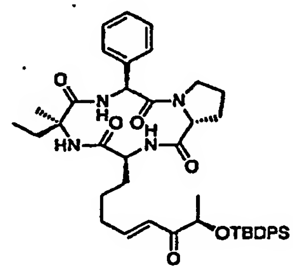
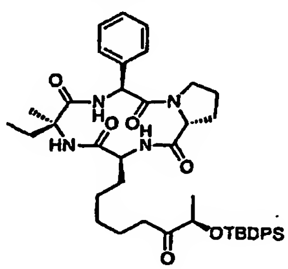
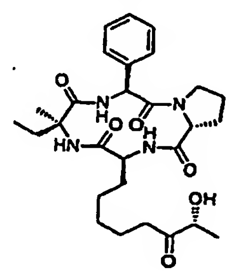
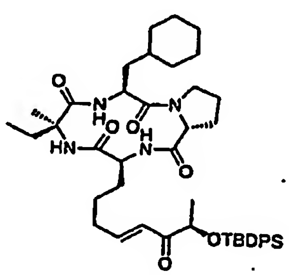
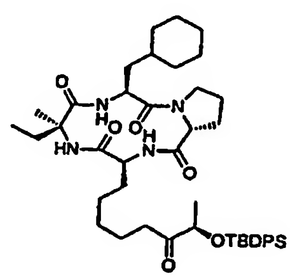
Compound E105	Compound E106
	
Compound E107	**Compound E108**
	
Compound E109	**Compound E110**
	
Compound E111	**Compound E112**
	

Table 2-51

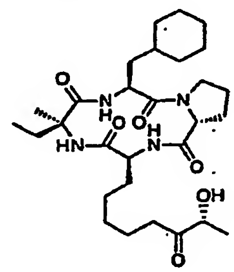
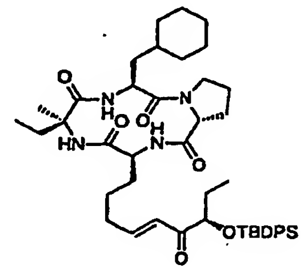
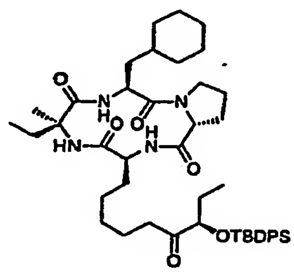
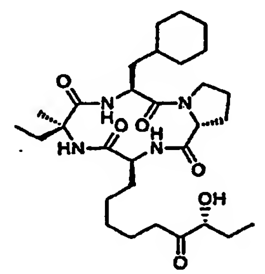
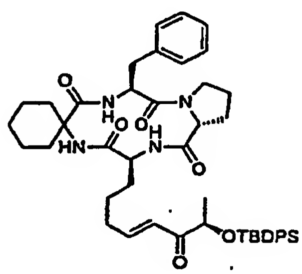
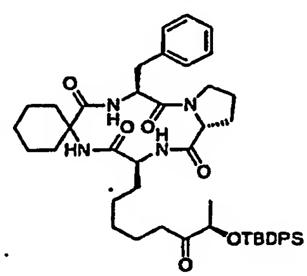
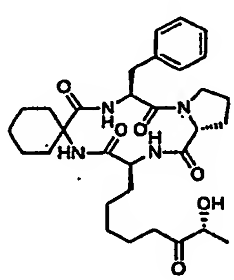
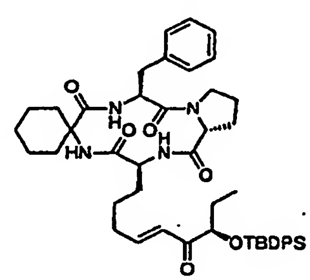
Compound E113	Compound E114
	
Compound E115	**Compound E116**
	
Compound E117	**Compound E118**
	
Compound E119	**Compound E120**
	

Table 2-52

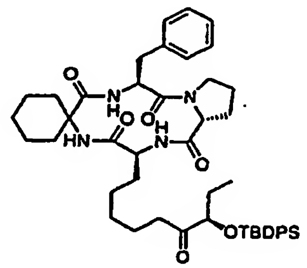
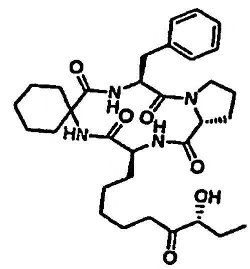
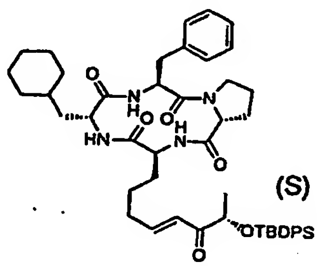
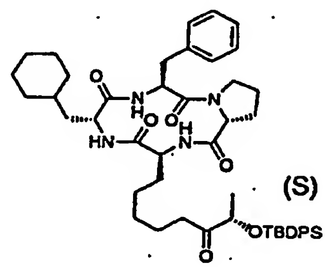
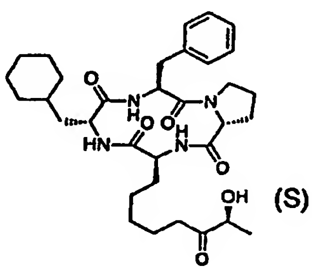
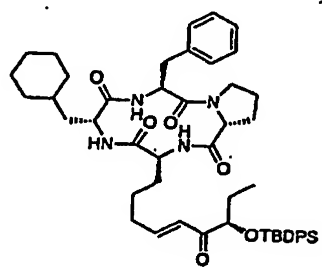
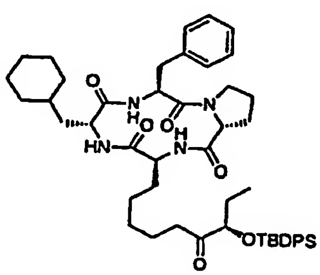
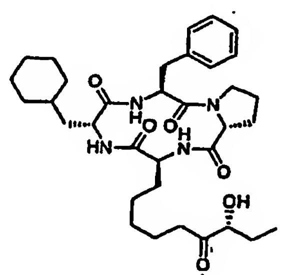
Compound E121	Compound E122
	
Compound E123	Compound E124
	
Compound E125	Compound E126
	
Compound E127	Compound E128
	

Table 2-53

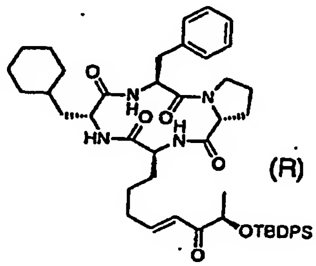
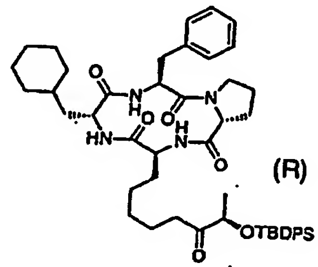
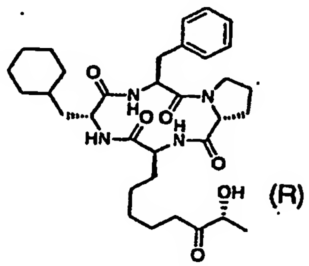
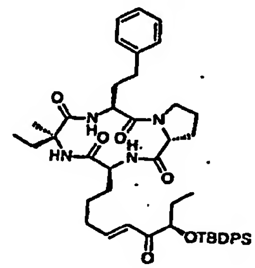
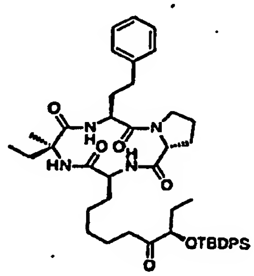
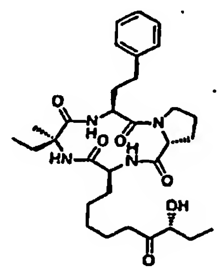
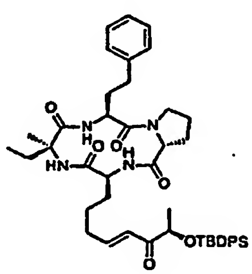
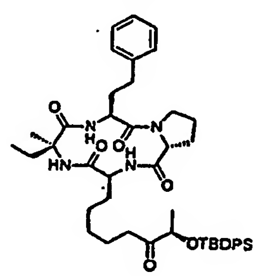
Compound E129	Compound E130
	
Compound E131	**Compound E132**
	
Compound E133	**Compound E134**
	
Compound E135	**Compound E136**
	

Table 2-54

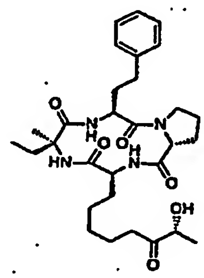
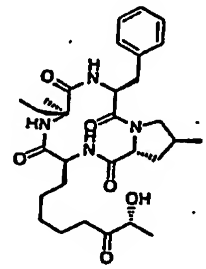
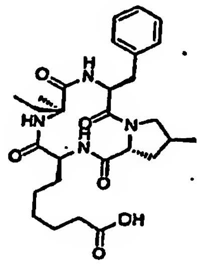
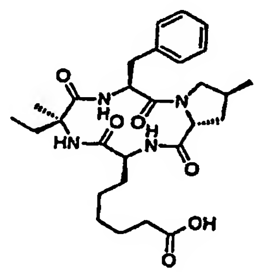
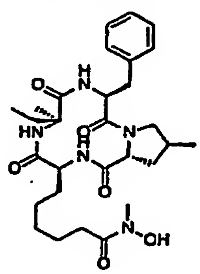
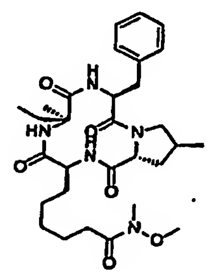
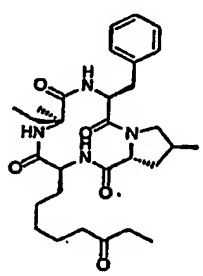
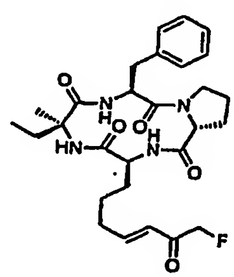
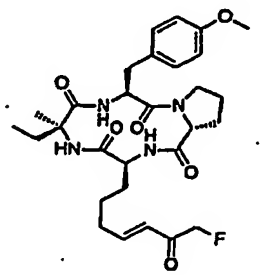
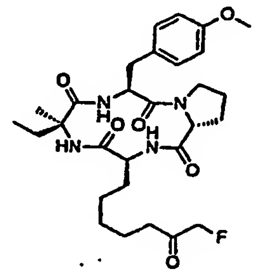
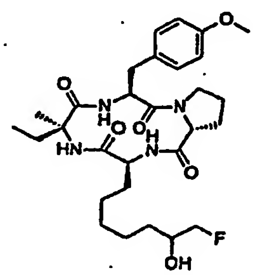
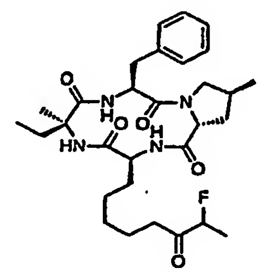
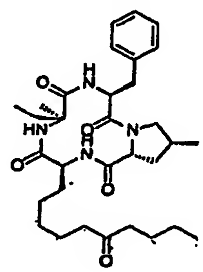
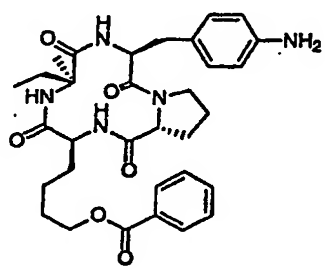
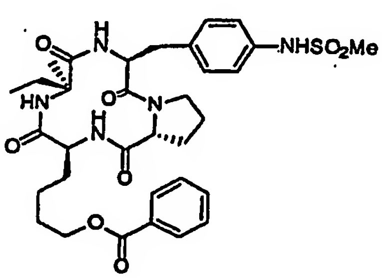
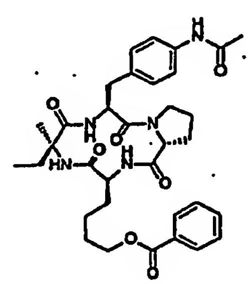
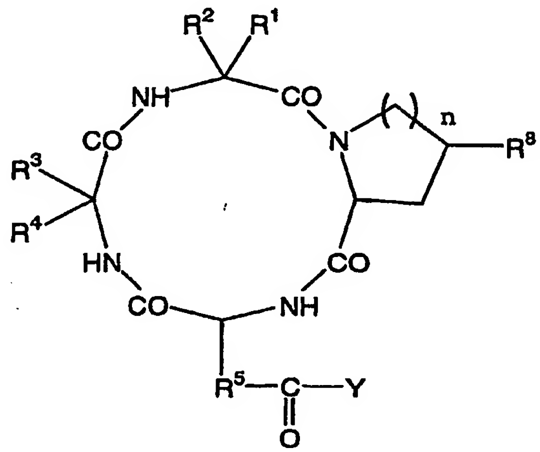
Compound E137	Compound E138
	
Compound E139	**Compound E140**
	
Compound E141	**Compound E142**
	
Compound E143	**Compound E144**
	

Table 2-55

Compound E145	Compound E146
	
Compound E147	Compound E148
	
Compound E149	Compound E150
	
Compound E151	Compound E152
	

CLAIMS

1. A cyclic tetrapeptide compound of the formula (I):



(I) .

wherein

R^1 is hydrogen,

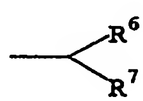
R^2 is lower alkyl, aryl, ar(lower)alkyl optionally substituted with one or more suitable substituent(s), heterocyclic(lower)alkyl or cyclo(lower)alkyl(lower)alkyl,

R^3 and R^4 are each independently hydrogen, lower alkyl, ar(lower)alkyl optionally substituted with one or more suitable substituent(s), heterocyclic(lower)alkyl optionally substituted with one or more suitable substituent(s) or cyclo(lower)alkyl(lower)alkyl, or

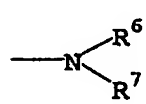
R^3 and R^4 are linked together to form lower alkylene or condensed ring,

R^5 is lower alkylene wherein at least one methylene of which is optionally replaced by oxygen atom(s), or lower alkenylene,

Y is hydroxy, aryl,



or



[wherein R^6 is hydrogen, halogen, hydroxy or protected hydroxy, and R^7 is hydrogen, halogen or lower alkyl],

R^8 is hydrogen or lower alkyl, and

n is an integer of 1 or 2,

providing that,

when R^3 is methyl, R^4 is methyl or ethyl, R^5 is pentylene and Y is

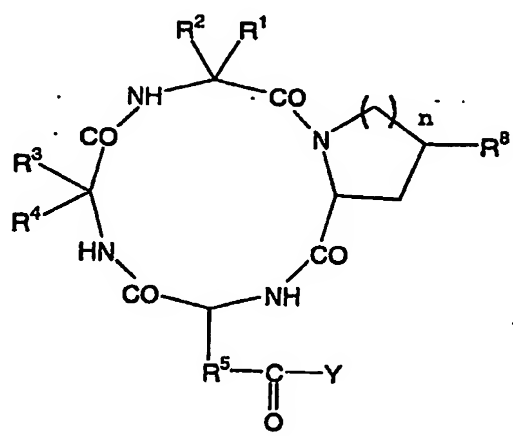
1-hydroxyethyl, then R^2 is phenyl(lower)alkyl substituted with one or more suitable substituent(s),
or a salt thereof.

2. The cyclic tetrapeptide compound of claim 1, wherein
R^2 is phenyl(lower)alkyl optionally substituted with one or more suitable substituent(s) selected from the group consisting of lower alkyl, lower alkoxy, ar(lower)alkyloxy, cyano, hydroxy, halogen, amino, acylamino, (lower)alkylsulfonylamino and phenyl,
R^3 and R^4 are each independently lower alkyl, and
R^5 is lower alkylene wherein at least one methylene of which is optionally replaced by oxygen atom(s).

3. A pharmaceutical composition containing the cyclic tetrapeptide compound of claim 1 or 2 as an active ingredient, in association with a pharmaceutically acceptable, substantially non-toxic carrier or excipient.

4. The cyclic tetrapeptide compound of claim 1 or 2 for use as a medicament.

5. A histone deacetylase inhibitor comprising a cyclic tetrapeptide compound of the formula (I):



(I)

wherein
R^1 is hydrogen,
R^2 is lower alkyl, aryl, ar(lower)alkyl optionally substituted with one or more suitable substituent(s), heterocyclic(lower)alkyl or

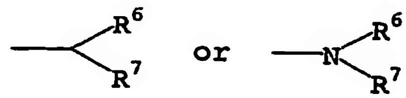
cyclo(lower)alkyl(lower)alkyl,

R^3 and R^4 are each independently hydrogen, lower alkyl, ar(lower)alkyl optionally substituted with one or more suitable substituent(s), heterocyclic(lower)alkyl optionally substituted with one or more suitable substituent(s) or cyclo(lower)alkyl(lower)alkyl, or

R^3 and R^4 are linked together to form lower alkylene or condensed ring,

R^5 is lower alkylene wherein at least one methylene of which is optionally replaced by oxygen atom(s), or lower alkenylene,

Y is hydroxy, aryl,



[wherein R^6 is hydrogen, halogen, hydroxy or protected hydroxy, and R^7 is hydrogen, halogen or lower alkyl],

R^8 is hydrogen or lower alkyl, and

n is an integer of 1 or 2,

providing that,

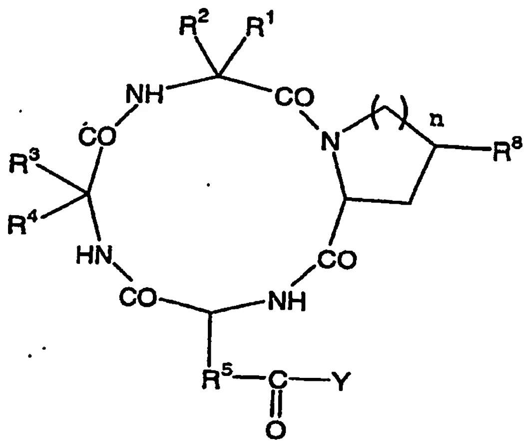
when R^3 is methyl, R^4 is methyl or ethyl, R^5 is pentylene and Y is 1-hydroxyethyl, then R^2 is phenyl(lower)alkyl substituted with one or more suitable substituent(s),

or a salt thereof.

6. A method for inhibiting histone deacetylase, comprising using a cyclic tetrapeptide compound (I) of claim 5.

7. A use of a cyclic tetrapeptide compound (I) of claim 5 for the manufacture of a medicament for inhibiting histone deacetylase.

8. A pharmaceutical composition for treating or preventing inflammatory disorders, diabetes, diabetic complications, homozygous thalassemia, fibrosis, cirrhosis, acute promyelocytic leukaemia (APL), organ transplant rejections, autoimmune diseases, protozoal infections or tumors, which comprises, as an active ingredient, a cyclic tetrapeptide compound of the formula (I):



(I)

wherein

R^1 is hydrogen,

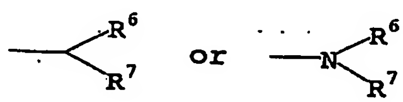
R^2 is lower alkyl, aryl, ar(lower)alkyl optionally substituted with one or more suitable substituent(s), heterocyclic(lower)alkyl or cyclo(lower)alkyl(lower)alkyl,

R^3 and R^4 are each independently hydrogen, lower alkyl, ar(lower)alkyl optionally substituted with one or more suitable substituent(s), heterocyclic(lower)alkyl optionally substituted with one or more suitable substituent(s) or cyclo(lower)alkyl(lower)alkyl, or

R^3 and R^4 are linked together to form lower alkylene or condensed ring,

R^5 is lower alkylene wherein at least one methylene of which is optionally replaced by oxygen atom(s), or lower alkenylene,

Y is hydroxy, aryl,



[wherein R^6 is hydrogen, halogen, hydroxy or protected hydroxy, and R^7 is hydrogen, halogen or lower alkyl],

R^8 is hydrogen or lower alkyl, and

n is an integer of 1 or 2,

providing that,

when R^3 is methyl, R^4 is methyl or ethyl, R^5 is pentylene and Y is 1-hydroxyethyl, then R^2 is phenyl(lower)alkyl substituted with one or more suitable substituent(s),

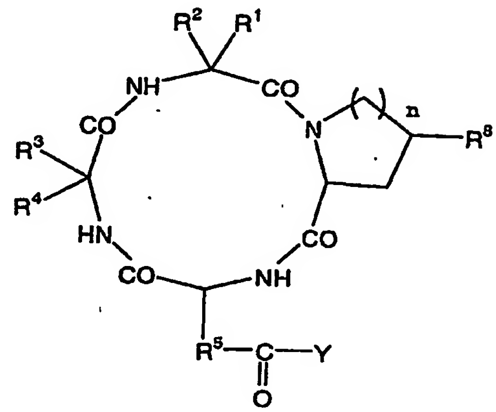
or a salt thereof.

9. A method for treating or preventing inflammatory disorders, diabetes, diabetic complications, homozygous thalassemia, fibrosis, cirrhosis, acute promyelocytic leukaemia (APL), organ transplant rejections, autoimmune diseases, protozoal infections or tumors, which comprises administering a cyclic tetrapeptide compound (I) of claim 8 to a human being or an animal.

10. A use of a cyclic tetrapeptide compound (I) of claim 8 for the manufacture of a medicament for treating or preventing inflammatory disorders, diabetes, diabetic complications, homozygous thalassemia, fibrosis, cirrhosis, acute promyelocytic leukaemia (APL), organ transplant rejections, autoimmune diseases, protozoal infections or tumors.

ABSTRACT

A cyclic tetrapeptide compound of the formula (I):



(I)

wherein R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, Y and n are as defined in the description, or a salt thereof;

a pharmaceutical composition containing the compound (I) as an active ingredient, in association with a pharmaceutically acceptable, substantially non-toxic carrier or excipient;

the compound (I) for use as a medicament;

a use of the compound (I) for manufacture of a medicament for inhibiting histone deacetylase;

a use of the compound (I) for manufacture of a medicament for treating or preventing inflammatory disorders, diabetes, diabetic complications, homozygous thalassemia, fibrosis, cirrhosis, acute promyelocytic leukaemia (APL), protozoal infections, organ transplant rejections, autoimmune diseases, or tumors;

a use of histone deacetylase inhibitors as an immunosuppressant or an antitumor agent; and

a use of histone deacetylase inhibitors for manufacture of a medicament for treating or preventing organ transplant rejections, autoimmune diseases, protozoal infections or tumors are described.